Claims

We claim:

1. Use of a myosin inhibitor in the manufacture of a medicament for the treatment of a patient having cardiac hypercontractility, impaired cardiac relaxation and/or left ventricular hypertrophy, wherein the patient is undergoing β blocker therapy,

wherein the patient is to be administered a therapeutically effective amount of a myosin inhibitor during a first treatment phase during which the patient also receives β blocker therapy; and

wherein the patient is to be administered a therapeutically effective amount of a myosin inhibitor during a second treatment phase during which the patient either (a) does not receive β blocker therapy, or (b) receives a reduced amount of β blocker therapy.

2. The use of claim 1, wherein the patient does not receive β blocker therapy during the second treatment phase.

3. The use of claim 1, wherein the patient receives a reduced amount of β blocker therapy during the second treatment phase.

4. The use of any preceding claim, wherein the myosin inhibitor is mavacamten or a pharmaceutically acceptable salt thereof.

5. The use of any preceding claim, wherein the patient has hypertrophic cardiomyopathy (HCM).

6. The use of any preceding claim, wherein the patient has obstructive hypertrophic cardiomyopathy (oHCM).

7. The use of any preceding claim, wherein the patient has non-obstructive hypertrophic cardiomyopathy (nHCM).

8. The use of any preceding claim, wherein the patient has heart failure with preserved ejection fraction (HFpEF).

9. Use of a myosin inhibitor in the manufacture of a medicament for the treatment of a patient having cardiac hypercontractility, impaired cardiac relaxation and/or left ventricular hypertrophy, wherein the patient is undergoing β blocker therapy,

wherein the β blocker therapy is discontinued or reduced in amount; and

wherein a therapeutically effective amount of a myosin inhibitor is to be administered to the patient.

10. The use of claim 9, wherein the β blocker therapy is discontinued.

11. The use of claim 9, wherein the amount of β blocker therapy is reduced.

12. The use of any one of claims 9-11, wherein the myosin inhibitor is mavacamten or a pharmaceutically acceptable salt thereof.

13. The use of claim 12, wherein the administration of a therapeutically effective amount of a myosin inhibitor to the patient comprises administration of a starting dose of 5 mg of mavacamten per day.

14. The use of claim 13, wherein the starting dose of 5 mg of mavacamten per day is adjusted or maintained based on the Valsalva or post-exercise LVOT gradient of the patient.

15. The use of claim 14, wherein the starting dose of mavacamten is reduced to 2.5 mg if the Valsalva or post-exercise LVOT gradient of the patient is less than 30 mmHg.

16. The use of claim 15, wherein the starting dose of mavacamten is reduced to 2.5 mg if the Valsalva or post-exercise LVOT gradient of the patient is less than 30 mmHg after 8 weeks of administering 5 mg of mavacamten per day.

17. The use of claim 14, wherein the starting dose of mavacamten is increased to 10 mg if the Valsalva or post-exercise LVOT gradient of the patient is greater than or equal to 30 mmHg.

18. The use of claim 17, wherein the starting dose of mavacamten is increased to 10 mg if the Valsalva or post-exercise LVOT gradient of the patient is greater than or equal to 30 mmHg after 8 weeks of administering 5 mg of mavacamten per day.

19. The use of any one of claims 9-18, wherein the patient has hypertrophic cardiomyopathy (HCM).

20. The use of claim 19, wherein the patient has obstructive hypertrophic cardiomyopathy (oHCM).

21. The use of claim 19, wherein the patient has non-obstructive hypertrophic cardiomyopathy (nHCM).

22. The use of any one of claims 9-18, wherein the patient has heart failure with preserved ejection fraction (HFpEF).

23. The use of any one of claims 9-22, wherein the patient is not suffering from one or more of, or is not suffering from any of: coronary artery disease (CAD), chest pain, angina, super ventricular arrhythmia, atrial fibrillation, congestive heart failure, left ventricular failure, stress cardiomyopathy, cardiac hypertension, ventricular tachycardia (VT), valvular disease, aortic stenosis, and coronary heart disease.

24. The use of any one of claims 9-23, wherein the β blocker therapy comprises administration of one or more β blockers selected from the group consisting of acebutolol, atenolol, betaxolol, bisoprolol, metoprolol, nadolol, nebivolol, propranolol, and sotalol.

25. The use of any one of claims 9-24, wherein the peak exercise capacity of the patient is increased and/or maximized.

26. The use of any one of claims 9-25, wherein the patient achieves an improvement in pVO_2 of at least about 2.2 mL/kg/min.

27. The use of any one of claims 9-26, wherein the patient achieves (i) an improvement of at least 1.5 mL/kg/min in pVO_2 and a reduction of 1 or more NYHA Class, or (ii) an improvement of at least 3.0 mL/kg/min in pVO_2 with no worsening in NYHA Class.

28. The use of any one of claims 9-27, wherein the patient has one or more of:

an ejection fraction >55% prior to administration of the myosin inhibitor;

an E/e' >14 prior to administration of the myosin inhibitor; and

a left ventricular wall thickness ≥15mm or ≥13 mm with family history of HCM prior to administration of the myosin inhibitor.

29. The use of any one of claims 9-28, wherein the patient with cardiac hypercontractility has ejection fraction of >55% and evidence of oHCM, HCM and/or heart failure symptoms prior to beginning the first treatment phase.

30. Use of a myosin inhibitor in the manufacture of a medicament for the treatment of a patient having cardiac hypercontractility, impaired cardiac relaxation and/or left ventricular hypertrophy, wherein the patient is not undergoing β blocker therapy,

wherein the patient is to be administered a therapeutically effective amount of a myosin inhibitor.

31. The use of claim 30, wherein the patient has never received β blocker therapy.

32. The use of claim 30, wherein the patient has previously received β blocker therapy but has not received β blocker therapy for at least 14 days prior to administration of the myosin inhibitor.

33. The use of claim 30, wherein the patient has previously received β blocker therapy but has not received β blocker therapy for at least 30, at least 60, or at least 90 days prior to administration of the myosin inhibitor.

34. The use of any one of claims 30-33, wherein the patient is an athlete or has an active lifestyle.

35. The use of any one of claims 30-34, wherein the myosin inhibitor is mavacamten or a pharmaceutically acceptable salt thereof.