CLAIMS

1. A method of treating or ameliorating an engraftment arrhythmia in a subject recipient of a cardiac graft of cardiomyocytes, the method comprising administering to the subject an effective amount of amiodarone and an effective amount of ivabradine.

2. The method of claim 1, wherein the cardiac graft of cardiomyocytes comprises *in vitro*-differentiated cardiomyocytes.

3. The method of claim 2, wherein the *in vitro*-differentiated cardiomyocytes are differentiated from induced pluripotent stem (iPS) cells or from embryonic stem (ES) cells.

4. The method of any of claims 1-3, wherein the cardiac graft of cardiomyocytes is derived from stem cells autologous to the subject.

5. The method of any of claims 1-3, wherein the cardiac graft of cardiomyocytes is derived from stem cells allogeneic to the subject.

6. The method of any one of claims 1-5, wherein the amiodarone and ivabradine are administered concurrently with the cardiac graft of cardiomyocytes.

7. The method of any one of claims 1-5, wherein administration of amiodarone is initiated prior to administration of the cardiac graft of cardiomyocytes.

8. The method of any one of claims 1-5, wherein administration of ivabradine is initiated prior to administration of the cardiac graft of cardiomyocytes.

9. The method of any one of claims 1-5, wherein administration of both amiodarone and ivabradine is initiated prior to administration of the cardiac graft of cardiomyocytes.

10. The method of any one of claims 1-5, wherein the administration of ivabradine is initiated concurrently with or after administration of the cardiac graft of cardiomyocytes.

11. The method of any one of claims 1-5, wherein the administration of amiodarone is initiated concurrently with or after administration of the cardiac graft of cardiomyocytes.

12. The method of any one of claims 1-11, wherein the administration of amiodarone is a single bolus administration.

13. The method of any one of claims 1-11, wherein the administration is continuous or repeated administration.

14. The method of any one of claims 1-13, wherein the administration is oral administration and/or intravenous injection.

15. The method of any one of claims 1-14, wherein the amiodarone is administered orally at a dose of 100-800 mg, three times per day.

16. The method of any one of claims 1-14, wherein the amiodarone is administered by IV bolus at a dose of 100-300 mg.

17. The method of any one of claims 1-15, wherein the amiodarone is administered to a serum concentration of 1.5 to 2.5 μg/ml.

18. The method of any one of claims 1-17, wherein the ivabradine is orally administered at a dose of 5 to 15 mg, twice per day.

19. The method of any one of claims 1-18, wherein the ivabradine is administered when there is tachycardia.

20. The method of any one of claims 1-19, wherein ivabradine is administered to maintain a resting heart rate of less than or equal to 150 beats per minute (bpm).

21. The method of any one of claims 1-20, wherein the administration of amiodarone and ivabradine reduces post-graft accelerated heart rate experienced by the graft recipient by at least 10% relative to a subject receiving a graft of the same type of cells in the absence of amiodarone and ivabradine administration.

22. The method of any one of claims 1-21, wherein the administration of amiodarone and ivabradine reduces the proportion of time in which the subject experiences engraftment arrhythmia by at least 10%

relative to a subject receiving a cardiac graft of cardiomyocytes of the same type of cardiomyocytes in the absence of amiodarone and ivabradine administration.

23. The method of any one of claims 1-22, wherein administration of amiodarone and ivabradine is short-term.

24. The method of any one of claims 1-22, wherein administration of amiodarone and ivabradine is terminated after engraftment arrhythmia burden reaches zero, without recrudescence of the arrhythmia.

25. A method of cardiomyocyte transplant, the method comprising:

a) administering *in vitro*-differentiated cardiomyocytes to cardiac tissue of a subject in need thereof;

b) administering to the subject an amount of amiodarone and an amount of ivabradine effective to reduce engraftment arrhythmia in the subject.

26. The method of claim 25, wherein engraftment arrhythmia is reduced in the subject relative to a subject receiving *in vitro*-differentiated cardiomyocytes without receiving amiodarone and ivabradine.

27. The method of any one of claims 25 or 26, wherein the *in vitro*-differentiated cardiomyocytes are differentiated *in vitro* from embryonic stem cells or from iPS cells.

28. The method of claim 27, wherein the iPS cells are autologous to the subject.

29. The method of claim 27, wherein the iPS cells are allogeneic to the subject.

30. The method of any one of claims 25-29, wherein the amiodarone and ivabradine are administered concurrently with the *in vitro*-differentiated cardiomyocytes.

31. The method of any one of claims 25-29, wherein administration of amiodarone is initiated prior to administration of the *in vitro*-differentiated cardiomyocytes.

32. The method of any one of claims 25-29, wherein administration of ivabradine is initiated prior to administration of the *in vitro*-differentiated cardiomyocytes.

33. The method of any one of claims 25-29, wherein administration of both amiodarone and ivabradine is initiated prior to administration of the *in vitro*-differentiated cardiomyocytes.

34. The method of any one of claims 25-29, wherein the administration of ivabradine is initiated concurrently with or after administration of the *in vitro*-differentiated cardiomyocytes.

35. The method of any one of claims 25-29, wherein the administration of amiodarone is initiated concurrently with or after administration of the *in vitro*-differentiated cardiomyocytes.

36. The method of any one of claims 25-35, wherein the administration of ivabradine is a single bolus administration.

37. The method of any one of claims 25-36, wherein the administration is continuous or repeated administration.

38. The method of any one of claims 25-37, wherein the administration is oral administration and/or intravenous (IV) injection.

39. The method of any one of claims 25-38, wherein the amiodarone is administered orally at a dose of 100-800 mg, three times per day.

40. The method of any one of claims 25-39, wherein the amiodarone is administered by IV bolus at a dose of 100-300 mg.

41. The method of any one of claims 25-40, wherein the amiodarone is administered to a serum concentration of 1.5 to 2.5 μg/ml.

42. The method of any one of claims 25-41, wherein the ivabradine is orally administered at a dose of 5 to 15 mg, twice per day.

43. The method of any one of claims 25-42, wherein the ivabradine is administered when there is tachycardia.

44. The method of any one of claims 25-43, wherein ivabradine is administered to maintain a resting heart rate of less than or equal to 150 beats per minute (bpm).

45. The method of any one of claims 25-44, wherein administration of amiodarone and ivabradine is short-term.

46. The method of any one of claims 25-45, wherein administration of amiodarone and ivabradine is terminated after engraftment arrhythmia burden reaches zero, without recrudescence of the arrhythmia.

47. The method of any one of claims 1-46, wherein about 10 million cardiomyocytes to about 10 billion cardiomyocytes are administered to the subject.

48. The method of any one of claims 1-47, wherein the subject is a human.

49. The method of any one of claims 1-48, wherein the subject has or is at risk for having a cardiovascular disease or a cardiac event.

50. The method of claim 49, wherein the cardiovascular disease or the cardiac event is selected from the group consisting of: atherosclerotic heart disease, myocardial infarction, cardiomyopathy, cardiac arrhythmia, valvular stenosis, congenital heart disease, chronic heart failure, regurgitation, ischemia, fibrillation, and polymorphic ventricular tachycardia.

51. A composition comprising *in vitro*-differentiated cardiomyocytes, amiodarone and ivabradine.

CLAIMS

1. Use of amiodarone and ivabradine in the preparation of a medicament for the treatment or amelioration of an engraftment arrhythmia in a subject recipient of a cardiac graft of cardiomyocytes, in which an effective amount of amiodarone and an effective amount of ivabradine are to be administered to the subject.

2. Use according to Claim 1, in which the cardiac graft of cardiomyocytes comprises *in vitro*-differentiated cardiomyocytes.

3. Use according to Claim 2, in which the *in vitro*-differentiated cardiomyocytes are differentiated from induced pluripotent stem (iPS) cells or from embryonic stem (ES) cells.

4. Use according to Claim 1, 2 or 3, in which the cardiac graft of cardiomyocytes is derived from stem cells autologous to the subject.

5. Use according to any preceding claim, in which the amiodarone and ivabradine are to be administered concurrently with the cardiac graft of cardiomyocytes.

6. Use according to any of Claims 1 to 4, in which administration of amiodarone and/or ivabradine is to be initiated prior to administration of the cardiac graft of cardiomyocytes.

7. Use according to any of Claims 1 to 4, in which the administration of ivabradine and/or amiodarone is to be initiated concurrently with or after administration of the cardiac graft of cardiomyocytes.

8. Use according to any preceding claim, in which amiodarone is to be administered as a single bolus administration.

9. Use according to any of Claims 1 to 7, in which the administration is to be continuous or repeated administration; or oral administration and/or intravenous injection.

10. Use according to any preceding claim, in which the amiodarone is to be administered orally at a dose of 100-800 mg, three times per day; by IV bolus at a dose of 100-300 mg; or to a serum concentration of 1.5 to 2.5 μg/ml.

11. Use according to any preceding claim, in which the ivabradine is to be orally administered at a dose of 5 to 15 mg, twice per day.

12. Use according to any preceding claim, in which the ivabradine is to be administered when there is tachycardia or to maintain a resting heart rate of less than or equal to 150 beats per minute (bpm).

13. Use according to any preceding claim, in which the administration of amiodarone and ivabradine reduces post-graft accelerated heart rate experienced by the graft recipient by at least 10% relative to a subject receiving a graft of the same type of cells in the absence of amiodarone and ivabradine administration.

14. Use according to any preceding claim, in which the administration of amiodarone and ivabradine reduces the proportion of time in which the subject experiences engraftment arrhythmia by at least 10% relative to a subject receiving a cardiac graft of cardiomyocytes of the same type of cardiomyocytes in the absence of amiodarone and ivabradine administration.

15. Use according to any preceding claim, in which administration of amiodarone and ivabradine is short-term; or terminated after engraftment arrhythmia burden reaches zero, without recrudescence of the arrhythmia.

16. Use of amiodarone and ivabradine in the preparation of a medicament for reducing engraftment arrhythmia in a subject undergoing a cardiomyocyte transplant, in which:

(a) *in vitro*-differentiated cardiomyocytes are to be administered to cardiac tissue of a subject in need thereof, and

(b) an amount of amiodarone and an amount of ivabradine effective to reduce engraftment arrhythmia in the subject are to be administered to the subject.

17. Use according to any preceding claim, in which about 10 million cardiomyocytes to about 10 billion cardiomyocytes are to be administered to the subject.

18. Use according to any preceding claim, in which the subject is a human.

19. Use according to any preceding claim, in which the subject has or is at risk for having a cardiovascular disease or a cardiac event selected from the group consisting of: atherosclerotic

heart disease, myocardial infarction, cardiomyopathy, cardiac arrhythmia, valvular stenosis, congenital heart disease, chronic heart failure, regurgitation, ischemia, fibrillation, and polymorphic ventricular tachycardia.

20. A composition comprising *in vitro*-differentiated cardiomyocytes, amiodarone and ivabradine.