

CLAIMS

1. A method for treating or preventing progressive heart failure in a subject, the method comprising administering to the subject a composition comprising cells, wherein the subject has Class II heart failure according to the New York Heart Association (NYHA) classification scale.
2. A method of reducing progression of heart failure in a subject, the method comprising administering to the subject a composition comprising cells, wherein the subject has Class II heart failure according to the New York Heart Association (NYHA) classification scale.
3. A method of reducing cardiac death in a subject with Class II heart failure according to the New York Heart Association (NYHA) classification scale, the method comprising administering to the subject a composition comprising cells.
4. A method of selecting heart failure patients for treatment with cell therapy, the method comprising i) assessing heart failure according to the New York Heart Association (NYHA) classification scale, and ii) selecting a subject having Class II heart failure according to NYHA, preferably, wherein the method comprises administering a composition comprising cells.
5. The method according to anyone of claims 1 to 4, wherein the subject's CRP level is elevated prior to administering cells.
6. The method of claim 5, wherein the subject's CRP level is ≥ 2 mg/L.
7. The method according to any one of claims 1 to 6, wherein the cells:
 - induce new blood vessel formation in target tissue, preferably wherein the cells promote arteriogenesis; and/or
 - secrete factors that protect at risk myocardium.

8. The method according to claim 1 or claim 2 which comprises the steps of: i) selecting a subject having Class II heart failure according to the New York Heart Association (NYHA) classification scale, and ii) administering to the subject a composition comprising cells which induce new blood vessel formation in target tissue.
9. The method according to any one of claims 1 to 8, wherein administering the composition inhibits the subject's progression to NYHA class III progressive heart failure.
10. The method according to any one of claims 1 to 9, wherein the subject's level of N-terminal pro-B-type natriuretic peptide (NT-proBNP) is:
less than 2200 pg/ ml, preferably less than 2000 pg/ml, prior to administering the cells; or,
between 1000 pg/ml and 2000 pg/ ml prior to administering the cells.
11. The method according to any one of claims 1 to 10, wherein the subject's C-reactive protein (CRP) level is <5 mg/L, preferably <4 mg/L.
12. The method according to any one of claims 1 to 11, wherein the subject's CRP level is between 1.5 and 5 mg/L.
13. The method according to any one of claims 1 to 12, wherein the subject has had a heart failure hospitalisation event over the previous 9 months.
14. The method according to any one of claims 1 to 13, wherein the subject has a LVEF of less than about 45%, preferably less than 40%.
15. The method according to any one of claims 1 to 14, wherein the subject has persistent left ventricular dysfunction.
16. The method according to any one of claims 1 to 15, wherein the subject's heart failure results from an ischemic event or from a non-ischemic event.

17. The method according to any one of claims 1, 2 or 5 to 16, wherein the subject has a reduced risk of cardiac death after treatment.
18. The method of claim 17, wherein the reduced risk is relative to risk of cardiac death in a subject with NYHA class III progressive heart failure.
19. The method according to any one of claims 1 to 18, wherein the subject has a reduced risk of ischemic MACE (MI or stroke) after treatment.
20. The method according to any one of claims 1 to 19, wherein the composition is administered transendocardially and/or intravenously.
21. The method according to any one of claims 1 to 20, wherein the cells are mesenchymal lineage precursor or stem cells (MLPSCs).
22. The method of claim 21, wherein the MLPSCs are STRO-1+.
23. The method according to claim 21, wherein the MLPSCs are mesenchymal stem cells (MSCs).
24. The method according to claim 21 or claim 22, wherein the MLPSCs are allogeneic.
25. The method according to any one of claims 21 to 24, wherein the cells are culture expanded.
26. The method according to claim 25, wherein the cells are TNAP+ before they are culture expanded.
27. The method according to any one of claims 21 to 26, wherein the cells have been cryopreserved.

28. The method according to any one of claims 1 to 27 which comprises administering between 1×10^7 and 2×10^8 cells.
29. The method according to any one of claims 1 to 28, wherein the composition further comprises Plasma-Lyte A, dimethyl sulfoxide (DMSO), human serum albumin (HSA).
30. The method according to any one of claims 1 to 29, wherein the composition further comprises Plasma-Lyte A (70%), DMSO (10%), HSA (25%) solution, the HSA solution comprising 5% HSA and 15% buffer.
31. The method according to any one of claims 1 to 30, wherein the composition comprises greater than 6.68×10^6 viable cells/mL.
32. The method according to any one of claims 1 to 25 or 27 to 31, wherein the composition comprises human bone marrow-derived allogeneic mesenchymal precursor cells (MPCs) isolated from bone mononuclear cells with anti-STRO-3 antibodies, expanded *ex vivo*, and cryopreserved.
33. A method of reducing risk of an ischemic event in a subject, the method comprising administering to the subject a composition comprising cells.
34. The method of claim 33, wherein the subject's CRP level is ≥ 2 mg/L
35. The method of claim 33 or 34, wherein the ischemic event is formation of an arterial occlusion.
36. The method of claim 33 or 34, wherein the ischemic event is formation of a cerebrovascular or cardiac occlusion.
37. The method of claim 33 or 34, wherein the ischemic event is a stroke or myocardial infarction.

38. The method according to any one of claims 33 to 37, wherein the subject has non-ischemic cardiomyopathy.
39. The method according to any one of claims 33 to 38, wherein the cells are administered transendocardially.
40. The method according to any one of claims 33 to 39, wherein the subject has Class II or Class III heart failure according to the New York Heart Association (NYHA) classification scale.
41. The method according to any one of claims 33 to 40, wherein the cells:
induce new blood vessel formation in target tissue, preferably wherein the cells promote arteriogenesis; and/or
secrete factors that protect at risk myocardium.
42. The method according to any one of claims 33 to 41, wherein the cells are mesenchymal lineage precursor or stem cells (MLPSCs).
43. The method according to any one of claims 33 to 42, wherein the subject's level of N-terminal pro-B-type natriuretic peptide (NT-proBNP) is between 1000 pg/ml and 2000 pg/ml prior to administering the cells.
44. The method according to any one of claims 33 or 35 to 44, wherein the subject's C-reactive protein (CRP) level is between 1.5 and 5 mg/L.
45. The method of claim 42, wherein the MLPSCs are one or more of STRO-1+, allogeneic, culture expanded, subject to cryopreservation.
46. The method according to claim 45, wherein the cells are culture expanded and express TNAP+ before they are culture expanded.

47. The method according to any one of claims 33 to 46 which comprises administering between 1×10^7 and 2×10^8 cells.
48. The method according to any one of claims 33 to 47, wherein the composition comprises Plasma-Lyte A (70%), DMSO (10%), HSA (25%) solution, the HSA solution comprising 5% HSA and 15% buffer.
49. The method according to any one of claims 33 to 48, wherein the composition comprises human bone marrow-derived allogeneic mesenchymal precursor cells (MPCs) isolated from bone mononuclear cells with anti-STRO-3 antibodies, expanded *ex vivo*, and cryopreserved.
50. A method for determining elevated risk of one or more of cardiac death, myocardial infarction or stroke in a subject, the method comprising measuring the level of CRP in a sample obtained from a subject, wherein elevated CRP indicates elevated risk of cardiac death, myocardial infarction or stroke.
51. The method of claim 50, wherein the subject has progressive heart failure.
52. The method of claim 51, wherein the subject has Class II progressive heart failure.
53. The method according to any one of claims 50 to 52, wherein a level of CRP ≥ 2 mg/L indicates elevated risk of cardiac death, myocardial infarction or stroke.
54. The method according to any one of claims 50 to 53, wherein the method determines elevated risk of cardiac death.
55. A method for treating or preventing progressive heart failure in a subject, the method comprising administering to the subject a composition comprising mesenchymal precursor lineage or stem cells, wherein the subject has Class II or Class III heart failure

according to the New York Heart Association (NYHA) classification scale and active inflammation.

56. A method of reducing progression of heart failure in a subject, the method comprising administering to the subject a composition comprising mesenchymal precursor lineage or stem cells, wherein the subject has Class II or Class III heart failure according to the New York Heart Association (NYHA) classification scale and active inflammation.
57. A method of reducing cardiac death in a subject with Class II or Class III heart failure according to the New York Heart Association (NYHA) classification scale active inflammation, the method comprising administering to the subject a composition comprising mesenchymal precursor lineage or stem cells.
58. A method of selecting heart failure patients for treatment with cell therapy, the method comprising i) assessing CRP levels and heart failure according to the New York Heart Association (NYHA) classification scale, and ii) selecting a subject having Class II or Class III heart failure according to NYHA and active inflammation, preferably, wherein the method comprises administering a composition comprising mesenchymal precursor lineage or stem cells.
59. The method according to anyone of claims 55 to 58, wherein active inflammation is determined based on the subject's CRP level.
60. The method of claim 59, wherein active inflammation is characterised by a CRP level ≥ 2 mg/L.

CLAIMS

1. Use of a composition comprising mesenchymal lineage precursor or stem cells (MLPSCs) in the preparation of a medicament for treating or preventing progressive heart failure in a subject, in which the subject has Class II heart failure according to the New York Heart Association (NYHA) classification scale, and in which the subject's CRP level is ≥ 2 mg/L.
2. Use according to Claim 1, in which the medicament reduces the subject's progression to NYHA class III progressive heart failure.
3. Use of a composition comprising mesenchymal lineage precursor or stem cells (MLPSCs) in the preparation of a medicament for reducing progression of heart failure in a subject, in which the subject has Class II heart failure according to the New York Heart Association (NYHA) classification scale, and in which the subject's CRP level is ≥ 2 mg/L.
4. Use of a composition comprising mesenchymal lineage precursor or stem cells (MLPSCs) in the preparation of a medicament for reducing cardiac death in a subject with Class II heart failure according to the New York Heart Association (NYHA) classification scale, in which the subject's CRP level is ≥ 2 mg/L.
5. Use according to any preceding claim, in which the medicament:
 - induces new blood vessel formation; and/or
 - secretes factors that protect at risk myocardium.
6. Use according to any preceding claim, in which the medicament inhibits the subject's progression to NYHA class III progressive heart failure.
7. Use according to any preceding claim, in which the subject's level of N-terminal pro-B-type natriuretic peptide (NT-proBNP) is:
 - less than 2200 pg/ml, preferably less than 2000 pg/ml, prior to administering the medicament; or,
 - between 1000 pg/ml and 2000 pg/ml prior to administering the medicament.
8. Use according to any preceding claim, in which the subject's C-reactive protein (CRP) level is < 5 mg/L.

9. Use according to any preceding claim, in which the subject's CRP level is between 1.5 and 4 mg/L.
10. Use according to any preceding claim, in which the subject has:
 - had a heart failure hospitalisation event over the previous 9 months;
 - 5 a LVEF of less than 45%;
 - a LVEF of less than 40%;
 - persistent left ventricular dysfunction; and/or
 - heart failure results from an ischemic event or from a non-ischemic event.
11. Use according to Claim 1, 2 or 4 to 10, in which the medicament reduces the subject's

10 risk of cardiac death after treatment.
12. Use according to Claim 11, in which the reduced risk is relative to risk of cardiac death in a subject with NYHA class III progressive heart failure.
13. Use according to any preceding claim, in which the medicament reduces the subject's risk of ischemic MACE (MI or stroke) after treatment.
- 15 14. Use according to any preceding claim, in which the medicament is formulated for administration transendocardially and/or intravenously.
15. Use according to any preceding claim, in which the MLPSCs are mesenchymal stem cells (MSCs).
16. Use according to any preceding claim, in which the MLPSCs are allogeneic.
- 20 17. Use according to any preceding claim, in which the composition further comprises Plasma-Lyte A, dimethyl sulfoxide (DMSO), human serum albumin (HSA).
18. Use according to any preceding claim, in which the composition comprises greater than 6.68×10^6 viable cells/mL.
19. Use according to any preceding claim, in which the medicament comprises human bone

25 marrow-derived allogeneic mesenchymal precursor cells (MPCs) isolated from bone mononuclear cells with anti-STRO-3 antibodies, expanded *ex vivo*, and cryopreserved.

20. Use of a composition comprising human bone marrow-derived allogeneic mesenchymal precursor cells (MPCs) isolated from bone mononuclear cells with anti-STRO-3 antibodies, expanded *ex vivo*, and cryopreserved in the preparation of a medicament for reducing risk of an ischemic event in a subject, in which the subject's CRP level is ≥ 2 mg/L.
- 5 21. Use according to Claim 20, in which the ischemic event is:
- formation of an arterial occlusion;
 - formation of a cerebrovascular or cardiac occlusion;
 - a stroke; or
 - a myocardial infarction.
- 10 22. Use according to Claim 20 or 21, in which the subject has non-ischemic cardiomyopathy and/or the subject has Class II or Class III heart failure according to the New York Heart Association (NYHA) classification scale.