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Claims

1. A dipeptidyl peptidase-4 (DPP-4) inhibitor, or a pharmaceutical composition containing said inhibitor, for use in:
- 5 (a) treating or preventing heart failure; or
(b) treating cardiac ischaemic reperfusion injury,
in a subject, wherein said subject has been administered extracorporeal cardiac shockwave therapy and wherein said inhibitor is for administration prior to, simultaneously with, and/or after administration of said shockwave therapy.
- 10 2. The DPP-4 inhibitor or composition for use according to claim 1, wherein said inhibitor or composition is provided as a combined preparation with a pharmacological agent suitable for mobilising stem cells for separate, simultaneous or sequential use or administration.
- 15 3. The DPP-4 inhibitor or composition for use according to claim 2, wherein said pharmacological agent suitable for mobilising stem cells is parathyroid hormone or a fragment thereof.
- 20 4. The DPP-4 inhibitor or composition for use according to claim 3, wherein said parathyroid hormone fragment comprises teriparatide.
- 25 5. The DPP-4 inhibitor or composition for use according to any one of claims 1 to 4, wherein said inhibitor or composition is for administration prior to said shockwave therapy administration continues throughout the course of the shockwave therapy.
- 30 6. The DPP-4 inhibitor or composition for use according to any one of claims 2 to 5, wherein the pharmacological agent suitable for mobilising stem cells is for administration at least 8 hours before the shockwave therapy.
7. The DPP-4 inhibitor or composition for use according to claim 1, wherein said inhibitor is provided as a combined preparation with stem cells for separate, simultaneous or sequential use or administration.

8. The DPP-4 inhibitor or composition for use according to claim 7, wherein said stem cells are derived from or comprise bone marrow-derived mononuclear cells.

5 9. The DPP-4 inhibitor or composition for use according to claim 6 or 7, wherein the stem cells are for administration at least 8 hours before the shockwave therapy.

10 10. The DPP-4 inhibitor or composition for use according to any one of claims 1 to 9, wherein the DPP-4 inhibitor is Sitagliptin, Linagliptin, Vildagliptin, Gemigliptin, Anagliptin, Teneligliptin, Trelagliptin, Dutogliptin, Omarigliptin, Lupeol or a combination thereof.

15 11. The DPP-4 inhibitor or composition for use according to any one of claims 1 to 10, wherein said heart failure is chronic heart failure or post-infarction heart failure.

20 12. The DPP-4 inhibitor or composition for use according to any one of claims 1 to 10, wherein said shockwave therapy comprises administration of shockwave pulses with energy of about 0.05-0.25 mJ/mm².

25 13. The DPP-4 inhibitor or composition for use according to any one of claims 1 to 12, wherein said shockwave therapy comprises administration of at least about 500 shockwave pulses, preferably at least about 1000 shockwave pulses.

30 14. The DPP-4 inhibitor or composition for use according to any one of claims 1 to 13, wherein said shockwave therapy comprises administration of a dose of about 500-2000 shockwave pulses.

35 15. The DPP-4 inhibitor or composition for use according to any one of claims 1 to 14, wherein said shockwave therapy comprises administration of shockwave pulses during the isovolumic contraction and/or isovolumic relaxation periods of the cardiac cycle.

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16. The DPP-4 inhibitor or composition for use according to any one of claims 1 to 15, wherein the focal point of the shockwave pulses is targeted to a specific region of the heart.

5 17. The DPP-4 inhibitor or composition for use according to claim 16, wherein the region of the heart to be targeted is determined by echocardiography (Echo) visualisation and/or electrocardiogram (ECG) pattern recognition.

10 18. The DPP-4 inhibitor or composition for use according to claim 16, wherein the region of the heart to be targeted is determined by magnetic resonance imaging.

15 19. The DPP-4 inhibitor or composition for use according to any one of claims 16 to 18, wherein specific region of the heart to be targeted comprises scar tissue.

20 20. The DPP-4 inhibitor or composition for use according to any one of claims 1 to 19, wherein the dose of shockwave pulses is for administration over more than one session.

21. A method of treating or preventing heart failure or treating cardiac ischaemic reperfusion injury comprising administering extracorporeal cardiac shockwave therapy and a DPP-4 inhibitor, or a pharmaceutical composition comprising said inhibitor, to a subject in need thereof, wherein said inhibitor or
25 composition is administered prior to, simultaneously with, and/or after administration of said shockwave therapy.

30 22. The method of claim 21 further comprising administering a pharmacological agent suitable for mobilising stem cells to said subject, wherein said agent is administered separately, simultaneously or sequentially to said inhibitor or composition.

35 23. The method of claim 22, wherein said pharmacological agent suitable for mobilising stem cells is parathyroid hormone or a fragment thereof.

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24. The method of claim 23, wherein said parathyroid hormone fragment comprises teriparatide.

5 25. The method of any one of claims 21 to 24, wherein said inhibitor or composition is administered prior to said shockwave therapy and continuously throughout the course of the shockwave therapy.

10 26. The method of any one of claims 21 to 25, wherein said pharmacological agent suitable for mobilising stem cells is administered at least 8 hours before the shockwave therapy.

15 27. The method of claim 21 further comprising administering stem cells to said subject, wherein said stem cells are administered separately, simultaneously or sequentially to said inhibitor or composition.

28. The method of claim 27, wherein said stem cells are administered at least 8 hours before the shockwave therapy.

20 29. The method of claim 27 or 28, wherein said progenitor cells are derived from or comprise bone marrow-derived mononuclear cells.

25 30. The method of any one of claims 21 to 29, wherein the DPP-4 inhibitor is Sitagliptin, Linagliptin, Vildagliptin, Gemigliptin, Anagliptin, Teneligliptin, Trelagliptin, Dutogliptin, Omarigliptin, Lupeol or a combination thereof.

31. The method of any one of claims 21 to 30, wherein said heart failure is chronic heart failure or post-infarction heart failure.

30 32. The method of any one of claims 21 to 31, wherein said shockwave therapy comprises administering shockwave pulses with energy of about 0.05-0.25 mJ/mm².

35 33. The method any one of claims 21 to 32, wherein said shockwave therapy comprises administering at least about 500 shockwave pulses, preferably at least about 1000 shockwave pulses.

34. The method any one of claims 21 to 33, wherein said shockwave therapy comprises administering a dose of about 500-2000 shockwave pulses.

5 35. The method of any one of claims 21 to 34, wherein said shockwave therapy comprises administering shockwave pulses during the isovolumic contraction and/or isovolumic relaxation periods of the cardiac cycle.

10 36. The method of any one of claims 21 to 35 comprising targeting the focal point of the shockwaves to a specific region of the heart.

15 37. The method of claim 36 further comprising determining the region of the heart to be targeted by echocardiography (echo) visualisation and/or electrocardiogram (ECG) pattern recognition.

 38. The method of claim 36 further comprising determining the region of the heart to be targeted by magnetic resonance imaging.

20 39. The method of any one of claims 36 to 38, wherein specific region of the heart to be targeted comprises scar tissue.

 40. The method of any one of claims 21 to 39, comprising administering the dose of shockwave pulses over more than one session.

25 41. A method of treating cardiac ischaemic reperfusion injury comprising administering extracorporeal cardiac shockwave therapy to a subject in need thereof.

30 42. The method of claim 41, wherein said shockwave therapy comprises administering shockwave pulses with energy of about 0.05-0.25 mJ/mm².

 43. The method of claim 41 or 42, wherein said shockwave therapy comprises administering at least about 500 shockwave pulses, preferably at least about 1000 shockwave pulses.

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44. The method of any one of claims 41 to 43 comprising administering shockwave pulses during the isovolumic contraction or isovolumic relaxation periods of the cardiac cycle.

5 45. The method of claim any one of claims 41 to 44 comprising targeting the focal point of the shockwaves to a specific region of the heart.

 46. The method of claim 45 further comprising determining the region of the heart to be targeted by echocardiography (echo) visualisation and/or
10 electrocardiogram (ECG) pattern recognition.

 47. The method of any one of claims 41 to 46, comprising administering the dose of shockwave pulses over more than one session.

15 48. A kit or product containing:
 (i) a DPP-4 inhibitor or composition comprising said inhibitor; and
 (ii) a pharmacological agent for mobilising stem cells, such as parathyroid hormone or fragment thereof, or a pharmaceutical composition comprising said pharmacological agent and at least one pharmaceutically acceptable carrier, diluent
20 or excipient; and optionally
 (iii) an additional agent, e.g. an agent for treatment of heart failure or glucose, or a pharmaceutical composition comprising said additional agent and at least one pharmaceutically acceptable carrier, diluent or excipient.

25 49. The kit or product of claim 48, wherein (i), (ii) and optionally (iii) are provided as a combined preparation for simultaneous, sequential or separate use in:

 (a) treating or preventing heart failure; or
 (b) treating cardiac ischaemic reperfusion injury,
30 in a subject, wherein said subject has been administered extracorporeal cardiac shockwave therapy and wherein said inhibitor and/or hormone is for administration prior to, simultaneously with, and/or after administration of said shockwave therapy.

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50. The kit or product of claim 49, wherein said a DPP-4 inhibitor, pharmacological agent for mobilising stem cells and/or shockwave therapy is as defined in any of the aforementioned claims.