TREATMENT OF SEXUAL DYSFUNCTION AND IMPROVEMENT IN SEXUAL QUALITY OF LIFE

FIELD OF THE INVENTION

[0001] The present invention relates to methods of treating sexual dysfunction, particularly female sexual dysfunction, and related disorders and conditions pertaining to sexual activity and sexual satisfaction, and methods to enhance sexual satisfaction, particularly female sexual satisfaction by administering therapeutically effective amounts of isolated populations of mesenchymal stem cells.

BACKGROUND OF THE INVENTION

[0002] Female sexual dysfunction (FSD) is a prevalent problem, afflicting approximately 40% of women. There are few treatment options. K.H. *et al., Cardiovasc Hematol Agents Med Chem. 7(4)*:260–269 (2009). FSD can be classified under many subtypes. For example, female sexual arousal disorder (FSAD) is a disorder characterized by a persistent inability to attain sexual arousal or to maintain arousal until the completion of a sexual activity. Female Sexual Interest/Arousal Disorder (FSIAD) is a diagnosis found when a subject experiences a lack of or significantly reduced sexual interest or arousal. Female hypoactive sexual desire disorder (FHSDD) is a general loss of interest in sexual activity. Other subtypes exist, for example, anorgasmia, a difficulty achieving orgasm. Currently, off-label use of testosterone has been prescribed. A therapy approved by the FDA in August 2015 is the Sprout Pharmaceuticals, Inc. product Addyi™ (flibanserin 100 mg), a once-daily, non-hormonal pill for the treatment of acquired, generalized hypoactive sexual desire disorder in premenopausal women. In addition, there are several drugs that were the subject of clinical trials that affect signaling in the brain. Wright, J.J. and O'Connor, K.M. *Medical Clinics of North America 99(3):*607-628 (2015). Because both hormonal and psycho-affective drugs can be associated with serious negative side effects, alternative treatment options are desired for treating this prevalent condition.

SUMMARY

[0003] The present disclosure concerns a method of increasing libido and/or sexual satisfaction in a patient, the method comprising administering to a patient in need thereof a

therapeutically effective amount of a population of isolated human mesenchymal stem cells. The present disclosure also concerns a method of treating sexual dysfunction in a patient, the method comprising administering to a patient in need thereof a therapeutically effective amount of a population of isolated human mesenchymal stem cells as either a short-term or a long-term therapy, wherein said sexual dysfunction is a sexual disorder selected from the group consisting of hypoactive sexual desire disorder, orgasmic disorder, and sexual arousal disorder.

[0003a] In one aspect, the present disclosure refers to a method of increasing libido and/or sexual satisfaction in a patient, the method comprising administering to a patient in need thereof a therapeutically effective amount of a population of isolated human mesenchymal stem cells, wherein the human mesenchymal stem cells do not express STRO-1.

[0003b] In another aspect, the present disclosure refers to the use of a therapeutically effective amount of a population of isolated human mesenchymal stem cells as either a short-term or a long-term therapy in the manufacture of a medicament for treating sexual dysfunction in a patient, comprising that a therapeutically effective amount of the population of isolated human mesenchymal stem cells is to be administered to the patient, wherein said sexual dysfunction is a sexual disorder selected from the group consisting of hypoactive sexual desire disorder, orgasmic disorder, and sexual arousal disorder; and wherein the human mesenchymal stem cells do not express STRO-1.

[0004] In one example of the disclosure, the sexual dysfunction is hypoactive sexual desire disorder. In another example of the disclosure, the patient is a human. In yet another example of the disclosure, the patient is a female.

[0005] In one example of the disclosure, the mesenchymal stem cells are bone marrow-derived mesenchymal stem cells, cord blood-derived mesenchymal stem cells, adipose tissue-derived mesenchymal stem cells, or derived from induced pluripotent stem cells (iPSCs). In one example of the disclosure, the mesenchymal stem cells do not express STRO-1. In another example of the disclosure, the mesenchymal stem cells do not express CD45. In another example of the disclosure, the mesenchymal stem cells do not express fibroblast surface markers or have a fibroblast morphology. In another example of the disclosure, the mesenchymal stem cells are not genetically manipulated. In some examples of the disclosure, the mesenchymal stem cells are allogeneic stem cells. In other examples of the disclosure, the mesenchymal stem cells are autologous stem cells. In yet other examples of

the disclosure, a mixture of allogeneic and autologous mesenchymal stem cells are administered to the patient. In yet additional examples of the disclosure, a mixture of mesenchymal stem cells and non-mesenchymal stem cells are administered to the patient.

[0006] In another example of the disclosure, the mesenchymal stem cells are administered in a single dose. In another example of the disclosure, the mesenchymal stem cells are administered in multiple doses, *e.g.,* two or more doses. In another example of the disclosure, the mesenchymal stem cells are administered at least yearly.

[0007] In one example, the mesenchymal stem cells are administered systemically. In one example of the disclosure, the mesenchymal stem cells are administered by infusion or direct injection. In one example of the disclosure, the mesenchymal stem cells are administered intravenously, intraarterially, intramuscularly, intraperitoneally, subcutaneously, intradermally, orally, transendocardially, or intranasally. In a further example, the mesenchymal stem cells are administered intravenously. In a further example, the mesenchymal stem cells are administered intramuscularly.

[0008] In one example of the disclosure, the mesenchymal stem cells are administered at a dose of about $20x10^6$ mesenchymal stem cells. In another example of the disclosure, the mesenchymal stem cells are administered at a dose of about $100x10^6$ mesenchymal stem cells.

[0009] In one example of the disclosure, the mesenchymal stem cells are obtained from a human donor and wherein a step of MHC matching of the human donor to the patient is not employed prior to the administration of the mesenchymal stem cells to the patient.

[0010] In one example of the disclosure, the treatment increases libido and/or sexual satisfaction or reduces sexual dysfunction in the patient by 25%.

BRIEF DESCRIPTION OF THE FIGURE(S)

[0011] FIG. 1. **Study Flow Chart.** The flow chart outlines how patients were screened and randomized for the CRATUS study.**[0012]** FIG. 2. **Sexual quality of life-female (SQOL-F) questionnaire.** There was a mean increase in the 100M-group ($p=0.0348$) from baseline to 6-months as compared to the 200M-group ($p=0.882$) and placebo ($p=0.941$). * indicates $p \leq 0.05$.

DETAILED DESCRIPTION

[0013] Embodiments may be practiced without the theoretical aspects presented. Moreover, the theoretical aspects are presented with the understanding that the embodiments are not bound by any theory presented.

[0014] Unless otherwise defined, all terms (including technical and scientific terms) used herein have the same meaning as commonly understood by one of ordinary skill in the art. It will be further understood that terms, such as those defined in commonly used dictionaries, should be interpreted as having a meaning that is consistent with their meaning in the context of the relevant art and will not be interpreted in an idealized or overly formal sense unless expressly so defined herein.

CLAIMS

l. A method of increasing libido and/or sexual satisfaction in a patient, the method comprising administering to a patient in need thereof a therapeutically effective amount of a population of isolated human mesenchymal stem cells, wherein the human mesenchymal stem cells do not express STRO-1.

2. Use of a therapeutically effective amount of a population of isolated human mesenchymal stem cells as either a short-term or a long-term therapy in the manufacture of a medicament for treating sexual dysfunction in a patient, comprising that a therapeutically effective amount of the population of isolated human mesenchymal stem cells is to be administered to the patient, wherein said sexual dysfunction is a sexual disorder selected from the group consisting of hypoactive sexual desire disorder, orgasmic disorder, and sexual arousal disorder; and wherein the human mesenchymal stem cells do not express STRO-1.

3. The use of claim 2, wherein said sexual dysfunction is hypoactive sexual desire disorder.

4. The method of claim 1, or the use of any one of claims 2-3, wherein the patient is a human.

5. The method of any one of claims 1 and 4, or the use of any one of claims 2-4, wherein the patient is a female.

6. The method of any one of claims 1, 4 and 5, or the use of any one of claims 2-5, wherein the mesenchymal stem cells are bone marrow-derived mesenchymal stem cells,

cord blood-derived mesenchymal stem cells, adipose tissue-derived mesenchymal stem cells, or derived from induced pluripotent stem cells (iPSCs).

7. The method of any one of claims 1 and 4-6, or the use of any one of claims 2-6, wherein the mesenchymal stem cells are allogeneic stem cells.

8. The method of any one of claims 1 and 4-6, or the use of any one of claims 2-6, wherein the mesenchymal stem cells are autologous stem cells.

9. The method of any one of claims 1 and 4-8, or the use of any one of claims 2-8, wherein the mesenchymal stem cells are to be coadministered with non-mesenchymal stem cells.

10. The method of any one of claims 1 and 4-9, or the use of any one of claims 2-9, wherein the mesenchymal stem cells do not express CD45.

11. The method of any one of claims 1 and 4-10, or the use of any one of claims 2-10, wherein the mesenchymal stem cells do not express fibroblast surface markers or have a fibroblast morphology.

12. The method of any one of claims 1 and 4-11, or the use of any one of claims 2-11, wherein the mesenchymal stem cells are not genetically manipulated.

13. The method of any one of claims 1 and 4-12, or the use of any one of claims 2-12, wherein the mesenchymal stem cells are to be administered in a single dose.

14. The method of any one of claims 1 and 4-12, or the use of any one of claims

2-12, ·wherein the mesenchymal stem cells are to be administered in two or more doses.

15. The method of any one of claims 1 and 4-14, or the use of any one of claims 2-14, ·wherein the mesenchymal stem cells are to be administered every 6 months.

16. The method of any one of claims 1 and 4-14, or the use of any one of claims 2-14, wherein the mesenchymal stem cells are to be administered at least yearly.

17. The method of any one of claims 1 and 4-16, or the use of any one of claims 2-16, wherein the mesenchymal stem cells are to be administered systemically.

18. The method of any one of claims 1 and 4-17, or the use of any one of claims 2-17, wherein the mesenchymal stem cells are to be administered by infusion or direct injection.

19. The method of any one of claims 1 and 4-18, or the use of any one of claims 2-18, wherein the mesenchymal stem cells are to be administered intravenously, intraarterially, or intraperitoneally.

20. The method or use of claim 19, wherein the mesenchymal stem cells are to be administered intravenously.

21. The method of any one of claims 1 and 4-20, or the use of any one of claims 2-20, wherein the mesenchymal stem cells are to be administered at a dose of about $20xl0^6$ mesenchymal stem cells.

22. The method of any one of claims 1 and 4-20, or the use of any one of claims

2-20, wherein the mesenchymal stem cells are to be administered at a dose of about $100x10^6$ mesenchymal stem cells.

23. The method of any one of claims 1 and 4-22, or the use of any one of claims 2-22, wherein the mesenchymal stem cells are to be obtained from a human donor and wherein a step of MHC matching of the human donor to the patient is not employed prior to the mesenchymal stem cells to be administered to the patient.

24. The method of any one of claims 1 and 4-23, or the use of any one claims 2-23, wherein treatment increases libido and/or sexual satisfaction or reduces sexual dysfunction in the patient by at least 25%.

25. The method or use of claim 24, wherein the increase in libido and/or sexual satisfaction or reduction in sexual dysfunction is measured according to a Sexual Quality Of Life-Female questionnaire.