SUMMARY

An objective of the present disclosure is to provide methods of treatment or alleviation for aging frailty in subjects in need thereof wherein these methods comprise administering a therapeutic amount of bone marrow derived mesenchymal stem cells to a subject in need.

In one aspect, the present disclosure provides a use of a composition comprising a therapeutically effective amount of bone marrow derived mesenchymal stem cells (MSCs) in the manufacture of a medicament for alleviating the symptoms of aging frailty in a subject in need thereof.

In another aspect, the present disclosure provides a use of a composition comprising a therapeutically effective amount of allogeneic mesenchymal stem cells (MSCs) in the manufacture of a medicament for treating aging frailty or inhibiting aging frailty disease progression.

Another objective of the present disclosure is to provide novel biomarkers for diagnosing and evaluating the progression of aging frailty in a subject in need thereof. These novel biomarkers can also be measured to determine the effectiveness of the treatment methods described herein.

Some examples are drawn to compositions comprising a therapeutically effective amount of bone marrow derived stem cells, specifically bone marrow derived mesenchymal stem cells (bMSCs), which are used to alleviate the symptoms of aging frailty, such as a decreased immune response or an increase in systemic inflammation. Other examples are drawn to methods of treatment wherein subjects suffering from symptoms of aging frailty are administered compositions comprising a therapeutically effective amount of bMSCs. The effectiveness of these treatments can be evaluated through measuring the concentrations and expression of specific biomarkers, such as Tie2, VEGF and TGF-β, in subjects after administration of compositions comprising bMSCs.

BRIEF DESCRIPTION OF DRAWINGS

FIG. 1 depicts a phase 2b, randomized, blinded and placebo-controlled clinical trial design for the evaluation of the safety and efficacy of Lomecel-B infusion in patients suffering from aging frailty.

FIG. 2A depicts a change in 6MWT versus time following treatment with Lomecel-B cells. All 4 Lomecel-B arms showed trending or significant increases in walk distance, in which the 200M dose showed the greatest changes from baseline. In contrast, the placebo arm showed a trending decrease by 9 months post-treatment. * = $p<0.05$ for change from baseline. ** = $p<0.01$ for change from baseline. # = $p<0.05$ for change from baseline of Lomecel-B arm versus change from baseline in placebo. ## = $p<0.01$ for change from baseline of Lomecel-B arm versus change from baseline in placebo.

FIG. 2B depicts the dose-response effect for each treatment group in FIG. 2A calculated using the MCP-Mod method. All five models were statistically significant, while the linear model yielded the smallest AIC value.

CLAIMS

1. Use of a composition comprising a therapeutically effective amount of bone marrow derived mesenchymal stem cells (MSCs) in the manufacture of a medicament for alleviating the symptoms of aging frailty in a subject in need thereof.

2. Use of a composition comprising a therapeutically effective amount of allogeneic mesenchymal stem cells (MSCs) in the manufacture of a medicament for treating aging frailty or inhibiting aging frailty disease progression.

3. The use according to claims 1 or 2, wherein the use further comprises that it is to be determined if a change occurs in the concentration of biomarkers in the subject suffering from symptoms of aging frailty before and after the administration of the composition comprising bone marrow derived MSCs.

4. The use according to claim 3, wherein the use further comprises that it is to be determined if an improvement occurs in the subject's functional mobility and/or exercise tolerance.

5. The use according to any one of claims 3-4, wherein the use further comprises that it is to be determined if an improvement occurs in the subject's ability to perform activities of daily living.

6. The use according to claim 5, wherein determining the improvement in the subject's ability to perform activities of daily living comprises examining the subject's PROMIS Physical Function score before and after administration of the bone marrow derived MSCs.

7. The use according to any one of claims 3 to 6, wherein the use further comprises that it is to be determined if an improvement occurs in the subject's PROMIS Mobility score.

8. The use according to any one of claims 3-7, wherein the use further comprises that it is to be determined if an improvement occurs in the subject's handgrip strength.

9. The use according to any one of claims 3-8, wherein the use further comprises that it is to be determined if an improvement occurs in the subject's gait or balance.

10. The use according to any one of claims 3-9, wherein the biomarkers comprise pro-inflammatory cytokines.

11. The use according to claim 10, wherein the pro-inflammatory cytokines are TNF-α, TGF-β, IL-1β, IL-2, D-dimer, C-reactive protein (CRP) or combinations thereof.

12. The use according to any one of claims 9-10, wherein the concentration of pro-inflammatory cytokines is decreased from 0.5% to 10%, 5% to 10%, 10% to 50%, or greater than 50% after administration of the composition comprising bone marrow derived MSCs.

13. The use according to any one of claims 3-12, wherein the biomarkers further comprise anti-inflammatory cytokines.

14. The use according to claim 13, wherein the anti-inflammatory cytokines are IL-8, soluble IL-2 receptor α (sIL-2Rα), IL-4, IL-10, IL-12, TNF-α stimulated gene 6 (TSG-6) or combinations thereof.

15. The use according to any one of claims 13 to 14, wherein the concentration of anti-inflammatory cytokines is increased from 0.5% to 10%, 5% to 10%, 10% to 50%, or greater than 50% after administration of the composition comprising bone marrow derived MSCs.

16. The use according to any one of claims 3-15, wherein the biomarkers further comprise soluble Tie2 (sTie2).

17. The use according to claim 16, wherein the concentration of sTie2 is decreased from 0.5% to 10%, 5% to 10%, 10% to 50%, or greater than 50% after administration of the composition comprising bone marrow derived MSCs.

18. The use according to any one of claims 3-17, wherein the biomarkers further comprise Tie2.

19. The use according to claim 18, wherein the concentration of Tie2 is increased from 0.5% to 10%, 5% to 10%, 10% to 50%, or greater than 50% after administration of the composition comprising bone marrow derived MSCs.

20. The use according to any one of claims 3-19, wherein the biomarkers further comprises VEGF.

21. The use according to claim 20, wherein the concentration of VEGF is increased from 0.5% to 10%, 5% to 10%, 10% to 50%, or greater than 50% after administration of the composition comprising bone marrow derived MSCs.