behavioral therapies, more effective treatments for children with ASD are needed, and there is a large unmet need for better, more effective and disease-modifying medical treatments for ASD. Human umbilical cord tissue-derived mesenchymal stromal cell (hCT-MSC) therapies may have potential to alleviate ASD symptoms by modulating inflammatory processes in the brain.

SUMMARY

[0013] The present disclosure provides methods of treating a patient suspected of having an autism spectrum disorder or a patient suffering from an autism spectrum disorder through the administration of human allogeneic umbilical cord tissue-derived mesenchymal stromal cells ("hCT-MSCs"). The present disclosure provides the benefit of eliminating the restriction of having a banked or otherwise available autologous cord blood unit.

[0014] In an example, the present disclosure comprises a method of treating a patient having or suspected of having an autism spectrum disorder, the method comprising administering a therapeutically effective amount of human allogeneic cord tissue-derived mesenchymal stromal cells (hCT-MSCs) to the patient. In certain examples, the hCT-MSCs are administered systemically. In some examples, they are administered intravenously. In some examples, they are administered by intravenous infusion over 30 minutes. In certain examples, the hCT-MSCs are administered in a single dose or multiple doses. In some examples, the hCT-MSCs are administered in one dose, two doses, three doses, or 4 or more doses. In certain examples, each dose is administered from about 1 month to about 6 months apart.

[0014a] In one aspect, the present disclosure refers to use of a therapeutically effective amount of human allogeneic cord tissue-derived mesenchymal stromal cells (hCT-MSCs) in the manufacture of a pharmaceutical composition for treating a patient having ~~or suspected of having~~ an autism spectrum disorder, wherein the patient is to be administered hCT-MSCs at a total amount of 6.0×10^6 cells/kg and is to be administered in 2 to 3 doses within 6 months.

[0015] In certain examples, the patient is administered hCT-MSCs at a dose of about 1.0×10^6 cells/kg to about 6.0×10^6 cells/kg. In certain examples, the patient is administered hCT-MSCs at a dose per dose about 2.0×10^6 cells/kg. In certain examples, the patient is administered hCT-MSCs at a dose per dose about 3.0×10^6 cells/kg. In certain examples, the patient is administered a total of 6.0×10^6 cells/kg in two to three doses within 6 months. In some examples, the dose comprises greater than 90% CD73+ and CD90+ cells. In some examples, the dose comprises less than 10% CD45+, CD3+, or CD31+ cells.

[0016] In another example, the present disclosure comprises a method of assessing the therapeutic effectiveness of treatment with hCT-MSCs on a patient suffering from an autism spectrum disorder comprising: (a) performing one or more appropriate tests on the patient to establish behavioral and/or biomarker baseline score(s); (b) administering an effective amount of hCT-MSCs to the patient; (c) reevaluating the patient at one or more time points post-administration of hCT-MSCs for the same one or more behavioral and/or biomarker tests set forth in (a); and (d) comparing the results in (c) with the baseline score(s)

established in (a). In certain examples of the disclosure, the behavioral test(s) performed in (a) and (c) comprise one or more of: Vineland Adaptive Behavior Scales-II (VABS-II), Vineland Adaptive Behavior Scales-III (VABS-III), Clinical Global Impression Scale (CGI), Pervasive Developmental Disorder Behavior Inventory (PDDBI), Expressive One-Word Picture Vocabulary Test-4 (EOWPVT-4), Aberrant Behavior Checklist, Sensory Experiences Questionnaire, Repetitive Behavior Scale, Intelligence Scales (Mullen Scales of Early Learning or Stanford-Binet), Language Environment Analysis, ATN GI Symptoms Inventory, and Parenting Stress Index. In certain examples of the disclosure, reevaluation of the patient in (c) is performed at one or more time point comprising: 2 months, 4 months, 6 months, 9 months, 12 months, and 18 months, 24 months, 2 years, 3 years, 4 years, 5 years, 10 years, 15 years, 20 years or indefinitely post-administration.

[0016a] In another aspect, the present disclosure refers to a method of assessing the therapeutic effectiveness of treatment with hCT-MSCs on a patient suffering from an autism spectrum disorder, said method comprising:

(a) establishing behavioral and/or biomarker baseline score(s) based on one or more appropriate behavioral and/or biomarker tests that have been performed on the patient;

(b) obtaining one or more post-treatment scores for the patient that has been administered ~~an effective amount of~~ hCT-MSCs at a total amount of 6.0×10^6 cells/kg, and is to be administered in 2 to 3 doses within 6 months and has been reevaluated at one or more time points post-administration of hCT-MSCs by the same one or more behavioral and/or biomarker tests set forth in (a); and

(c) comparing the results in (b) with the baseline score(s) established in (a), wherein an improved score in step (b), relative to the baseline score in step (a), indicates that the treatment is effective.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] FIG.1 shows the study design for Phase I study of hCT-MSC in children with ASD.

[0018] FIG.2 shows a summary of adverse events observed during Phase I hCT-MSC Study. A total of 3/53 (5.7%) events were related to study product—Hypotension and Infusion Related Reaction.

[0019] FIG.3A - 3B show general study designs for a Phase II study of hCT-MSC in children with ASD.

[0020] FIG.4 shows exemplary flow cytometry analysis of the hCT-MSC population for infusion. The populations are greater 90% CD73+ and CD90+, with less than 10% CD45+, CD3+, or CD31+.

DETAILED DESCRIPTION OF THE INVENTION

[0021] Before the disclosed processes and materials are described, it is to be understood that the aspects described herein are not limited to specific embodiments, apparati, or configurations, and as such can, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular aspects only and, unless specifically defined herein, is not intended to be limiting.

[0022] It is also to be understood that unless clearly indicated otherwise by the context, embodiments disclosed for one aspect or embodiment of the invention can be used in other aspects or embodiments of the invention as well, and/or in combination with embodiments disclosed in the same or other aspects of the invention. Thus, the disclosure is intended to include, and the invention includes, such combinations, even where such combinations have not been explicitly delineated.

CLAIMS

We claim:

1. Use of a therapeutically effective amount of human allogeneic cord tissue-derived mesenchymal stromal cells (hCT-MSCs) in the manufacture of a pharmaceutical composition for treating a patient having ~~or suspected of having~~ an autism spectrum disorder, wherein the patient is to be administered hCT-MSCs at a total amount of 6.0×10^6 cells/kg and is to be administered in 2 to 3 doses within 6 months.

2. The use of claim 1, wherein the pharmaceutical composition is to be administered systemically.

3. The use of claim 2, wherein the pharmaceutical composition is to be administered intravenously.

4. The use of any of claims 1-3, wherein the patient is from ~~about~~ 1 year old to ~~about~~ 45 years old.

5. The use of claim 4, wherein the patient is from ~~about~~ 2 years old to ~~about~~ 11 years old.

6. The use of claim 4, wherein the patient is from ~~about~~ 4 years old to ~~about~~ 8 years old.

~~7. The use of any of claims 1-6, wherein the pharmaceutical composition is to be administered in one dose, two doses, three doses, or 4 or more doses.~~

~~8. The use of any of claims 1-7, wherein each dose is to be administered from about 1 month to about 6 months apart.~~

~~9~~7. The use of ~~claim 8~~any of claims 1-6, wherein each dose is to be administered ~~about~~ two months apart.

~~10. The use of any of claims 1-9, wherein the therapeutically effective dose comprises about 1.0×10^6 hCT-MSCs/kg to about 6.0×10^6 hCT-MSCs/kg of body weight.~~

~~11. The use of claim 10, wherein the dose comprises about 2.0×10^6 hCT-MSCs/kg of body weight.~~

~~12. The use of claim 10, wherein the dose comprises about 3.0×10^6 hCT-MSCs/kg of body weight.~~

~~13. The use of claim 10, wherein the dose comprises about 6.0×10^6 hCT-MSCs/kg of body weight.~~

~~14. The use of any of claims 1-6, wherein the therapeutically effective dose comprises a total of about 6.0×10^6 hCT-MSCs/kg of body weight, and is to be administered in 2 to 3 doses within about 6 months.~~

~~15~~8. The use of any of claims 1-~~14~~7, wherein the therapeutically effective dose comprises greater than 90% CD73+ and CD90+.

~~16~~9. The use of any of claims 1-~~14~~7, wherein the therapeutically effective dose comprises less than 10% CD45+, CD3+, or CD31+.

~~17~~10. A method of assessing the therapeutic effectiveness of treatment with hCT-MSCs on a patient suffering from an autism spectrum disorder, said method comprising:

(a) establishing behavioral and/or biomarker baseline score(s) based on one or more appropriate behavioral and/or biomarker tests that have been performed on the patient;

(b) obtaining one or more post-treatment scores for the patient that has been administered ~~an effective amount of~~ hCT-MSCs at a total amount of 6.0×10^6 cells/kg, and is to be administered in 2 to 3 doses within 6 months and has been reevaluated at one or more time points post-administration of hCT-MSCs by the same one or more behavioral and/or biomarker tests set forth in (a); and

(c) comparing the results in (b) with the baseline score(s) established in (a), wherein an improved score in step (b), relative to the baseline score in step (a), indicates that the treatment is effective.

~~18~~11. The method of claim ~~17~~10, wherein the behavioral test(s) performed in (a) and (c) comprise one or more of: Vineland Adaptive Behavior Scales-II (VABS-II), Vineland Adaptive Behavior Scales-III (VABS-III), Clinical Global Impression Scale (CGI), Pervasive Developmental Disorder Behavior Inventory (PDDBI), Expressive One-Word Picture Vocabulary Test-4 (EOWPVT-4), Behavior Assessment for Children-Social Skills subscale, Aberrant Behavior Checklist, Sensory Experiences Questionnaire, Repetitive Behavior Scale, Intelligence Scales (Mullen Scales of Early Learning or Stanford-Binet), Language

Environment Analysis, Preschool Age Psychiatric Assessment, ATN GI Symptoms Inventory, and Parenting Stress Index.

~~19~~12. The method of claim ~~17~~10, wherein the biomarker test(s) performed in (a) and (c) comprise one or more of: Eye Gaze Tracking of Social Stimuli (EGT), Electroencephalogram (EEG), Computer Vision Analysis (CVA), and brain Magnetic Resonance Imaging (MRI).

~~20~~13. The method of any of claims ~~17~~10-~~19~~12, wherein reevaluation of the patient in (b) is performed at one or more time points comprising: 2 months, 4 months, 6 months, 9 months, 12 months, 18 months, 24 months, 2 years, 3 years, 4 years, 5 years, 10 years, 15 years, 20 years or indefinitely post-administration.