	IRCM-2022-330	April 27, 2022

A Retrospective Study to Evaluate the Safety of Cultured Human Wharton's Jelly Mesenchymal Stem Cell Therapy provided at BHI Slovakia

Protocol Identifying Number BHI22-WJMSC-SVK
Date March, 2021
Principal Investigator: Brian Mehling, MD
Study Coordinator: Doreen Santora

Sponsor
Blue Horizon International, LLC
330 E 38th St, PH 57JK,
New York, NY 10016

Table of Contents

PROTOCOL SUMMARY

1.1 Study Rationale

This protocol is for a retrospective study to evaluate the safety of Human Wharton's Jelly cultured mesenchymal stem cells (WJ-MSCs) administered via intravenous, intrathecal or intraarticular injection.

1.2 Study Design Overview

This retrospective study is designed to characterize the safety of WJ-MSC therapy in 13 subjects treated for a range of disease indications at Blue Horizon Internal (BHI) clinical site in Slovakia during the period between June 2020 – June 2021. Each subject's treatment process was documented, and the incidence of adverse events (AE) will be evaluated. Participants received conventional treatment for their specific indications. In addition, 1-2 treatments per subject of WJ-MSCs therapy was administered. During the follow up time, no severe treatment related adverse events were reported. Patient records and clinical outcomes will be evaluated retrospectively to evaluate the safety of WJ-MSC therapy.

1.3 Study Endpoints

Subjects will be followed on for 1 year to assess the safety of WJ-MSC therapy.
Safety endpoints:

- The incidence of adverse events (AEs), including clinical laboratory tests (serum chemistry, hematology, and urinalysis), vital signs (blood pressure, pulse, oral temperature, respiratory rate, and pulse oximetry), 12-lead electrocardiogram (ECG), and physical examination findings, were recorded during the follow-on period.

2 Background

2.1 Rationale Background

Mesenchymal stem/stromal cells (MSCs) are the leading candidate for regenerative medicine applications due to their established immunomodulatory ability, hypo-immunogenicity, regenerative capabilities and proven clinical safety. MSCs are multipotent, non-hematopoietic and have the capability for self-renewal and differentiation. MSCs can be isolated from many different tissues, most commonly bone-marrow, adipose, or umbilical cord (cord blood or Wharton's Jelly) origins [1–4]. The therapeutic effect of MSC therapy arises largely through immunomodulatory repair mechanisms. MSCs detect and home to sites of inflammation and damage [5,6] where they exhibit a dose-dependent antiproliferative effect on T and B lymphocytes, dendritic cells and natural killer

cells [7,8]. The reduction in local inflammation at the injury site provides a suitable environment for repair, which is furthered by secretion of trophic factors from MSCs that promote cell survival [9], angiogenesis [10] and accelerate tissue regeneration [11]. The pharmacokinetic characteristics and in vivo biodistribution of intravenous MSC delivery is well defined and non-toxic in many species, including dogs [12], rat [13], mice [14], sheep [15], and non-human primates [5,16,17]. These studies have characterized how MSCs distribute immediately under normal physiological conditions to the lungs after intravenous infusion, and later are found in the liver, spleen, bone marrow and kidneys[13,14,16]. If injury or inflammation is present, MSCs will subsequently migrate to the leading areas of damage, as identified in the injured muscle, skin, bone marrow, thymus and gut following total body irradiation in non-human primate[5,16,17].

Safety is the paramount concern during the development of any new therapeutic intervention. Human MSC (hMSC) therapy presents an impeccable safety profile. A meta-analysis of 36 clinical trials of human MSC therapy reported no serious adverse reactions, including no association with acute toxicity, thromboembolism, abnormal cell growths, neurological deterioration, or death [18]. This study reported the only adverse reaction as transient fever occurring in a subset of patients to a particular preparation of MSCs, with no long-term health concern. Further studies exemplify the safety of hMSC therapy which is routinely used with no severe adverse reactions reported [19–24]. Further, hMSC therapy presents no health concerns over long term follow ups. A 5-year study post hMSC treatment in stroke patients has reported no significant adverse reactions observed in the treatment group versus the control [25].

Blue Horizon International Therapeutics (BHIT) has to date treated thousands of patients with hMSCs without any serious adverse events. Published research from BHIT treatments continues to contribute to the expanding safety data supporting the use of hMSCs for a range of human conditions. We recently published a retrospective cohort study to evaluate the safety and efficacy of adipose tissue derived MSC therapy for osteoarthritis [26]. Evaluation of 350 patients receiving the therapy showed a significant improvement in pain levels and mobility, and critically, reported no severe adverse events or complications. Prior, we published data on the safety of MSC-containing cord blood therapy in 30 patients with spinal cord injury [27]. No subjects developed adverse reactions, further demonstrating the safety of hMSC therapy. Our clinical trial data for autologous MSC therapy as a spinal cord injury treatment in 20 patients reported no severe adverse effects [28]. The most common adverse event, fever and headache, disappeared without treatment within 24 to 48 hours. To provide further safety and immunogenicity data, we characterized the blood profile and immune response in 29 patients receiving human umbilical cord blood derived MSC treatment for chronic inflammation [29,30]. Our data demonstrated that no essential changes in blood markers (including general health blood test panel and inflammatory markers) occurs following stem cell treatment and when followed up for 3 months.

BHIT continues to be a world-leader in stem cell therapy by successfully treating patients world-wide and publishing data on the safety and efficacy of these interventions. BHIT is expanding its clinical indications for Blue Horizon stem cell therapy using Wharton's Jelly derived MSCs (WJ-MSCs). The use of allogenic WJ-MSCs has many advantages over autologous MSCs in which a patient's own cells are harvested from bodily stores. This includes circumventing the pain and healing process of invasive stem cell harvesting from a patient. Furthermore, MSCs of umbilical cord Wharton's Jelly origin offer the highest level of potency for therapeutic benefit as they exist in a more naive state than adult MSCs, and thus exhibit increased proliferation ability and anti-inflammatory effects [31]. Specifically, WJ-MSC administration is safe and effective for many indications, including in COVID-19 [32], acute graft versus host disease [33], and type 2 diabetes [34], where long term safety was confirmed over a 3 year follow on. Further, WJ-MSCs elicit no infusion-related toxicity, no development of treatment related adverse events, nor ectopic tissue formation even at high dosages [33,35]. In this study, we confirm the safety of human allogeneic WJ-MSCs delivered at a high dose (administration of 1 x 10^8 cells total), via multiple delivery routes (intravenous (IV), intrathecal (IT) or intraarticular (IA)), and in conjunction with Mannitol in some cases, for the treatment of various indications. Mannitol is a blood-brain barrier permeabilizer that can facilitate intravenously delivered stem cells to exert therapeutic benefits on the central nervous system, significantly improving recovery in pre-clinical stroke and traumatic brain injury. Therefore, Mannitol provides a useful adjunct for subjects unable to tolerate intrathecal administration.

2.2 Current standard of care

Many of the indications treated for in this retrospective study have unmet clinical needs and no curative solution, including stroke, osteoarthritis, spinal cord injury and hypoxic brain injury. Current treatments, such as for osteoarthritis, rely on merely treating the symptoms and alleviating pain rather than treating the pathological cause. WJ-MSCs offer a promising approach for a more long-term treatment option that can both regenerate the damaged organ, reduce inflammation and as a result alleviate pain.

2.3 Risk factors

There are no risks associated with this protocol as it is a retrospective case study analysis of treated patients. No treatment related severe adverse events were reported during the completed study period. The breach of confidentiality will be avoided by the procedures described in the section "Patient Information Confidentiality".

3 Subject population

3.1 Subject characteristics

This retrospective case study will evaluate 13 subjects treated at BHI Slovakia (Nemocnica Malacky hospital (Slovakia) between June 2020 – June 2021 (table 1).

Table 1. Treated Subject Characteristics and dosage regime

Subject ID	Age	Sex	Diagnosis	Doses	Delivery	Adverse events
SK1	78	M	Vascular insufficiency, diabetic wounds	2 (6 months apart)	Locally + IV	No
SK2	24	M	Spinal cord injury	2 (3 months apart)	IV + IT	No
SK3	64	F	Stroke	1	IV + IT	Headache
SK4	61	M	Stroke	1	IV + IT	No
SK5	58	M	Stroke, Myocardial infarction	2 (6 months apart)	IV + IT	No
SK6	3.5	M	Hypoxic brain injury	2 (3 months apart)	IV + IT	No
SK7	26	M	Spinal cord injury	2 (7 months apart)	IV + IT	No
SK8	63	F	Knee Osteoarthritis	1	IA	No
SK9	59	F	Knee & Hip Osteoarthritis	1	IA	No
SK10	56	M	Knee Osteoarthritis	1	IA	No
SK11	43	M	Hip Osteoarthritis	1	IA	No
SK12	34	M	Knee Osteoarthritis	1	IA	No
SK13	41	M	Knee Osteoarthritis	1	IA	No

M = Male, F = Female, IV = Intravenous, IT = Intrathecal, IA = Intraarticular

3.2 Inclusion/ Exclusion Criteria

This protocol has no prospective Inclusion/ Exclusion Criteria as it is a retrospective case study analysis of already treated patients. Inclusion/ Exclusion criteria was specified and approved at the time of patient enrolment at each study site. The criteria was specific to each disease condition but consisted of a base criteria as follows:
Inclusion Criteria:

- Age: 18+
- Life expectancy: Greater than 3 months

- Subjects' routine blood test, liver function and kidney function have no obvious abnormalities
- Ability to understand the study protocol and a willingness to sign a written informed consent document

Exclusion Criteria:

- Known or suspected allergy to the investigational agent or any agent given in association with this trial
- Pregnant or lactating subjects
- Active Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV) or Treponema Pallidum (Syphilis) infection
- Subjects who are suffering from serious autoimmune disease
- Subjects with current malignancy
- Subjects who has organ transplantation
- Now or recently will join another experimental clinical study
- Other situations that the researchers considered unsuitable for this study

3.3 Enrollment

Subjects were recruited into the study from associates of Blue Horizon International, clinic's previous subjects, referrals from other physicians, subject advocacy groups, direct website inquiries, and public outreach informational events.

3.4 Risk factors

There are no risks associated with this protocol as it is a retrospective case study analysis of treated patients. No severe treatment related adverse events were reported during the completed study period. There were 4 incidences of mild adverse events (chills, headaches, chest pain) reported during the study which resolved themselves without clinical concern The breach of confidentiality will be avoided by the procedures described in the section "Patient Information Confidentiality".

3.5 Process of consent

Informed consent was obtained through signature of an informed consent form from both patients during the enrolment stage of the study. The risks, benefits and alternatives of the therapy were explained both verbally and in writing to the subjects and all questions of the subjects were discussed.

3.6 Data confidentiality

The investigator affirms and upholds the principle of the subject's right to protection against invasion of privacy. Each subject was provided with a study number. No names will be listed in

our study. Information was and will be stored the same way as medical charts are stored according to HIPAA compliances. Subject names will be removed prior to submitting to any third party for review in order to maintain subject confidentiality. However, in compliance with the guidelines concerning the acceptance of clinical studies in support of an NDA and the ICH Guidelines (whether performed in the United States or elsewhere), the investigator will permit its study monitor, representatives from IRBs, and other governmental regulatory authorities to review the subject's primary medical records (source data or documents). Should access to such medical records require a waiver or authorization separate from the statement of informed consent, the investigator will obtain such permission in writing from the subject before the subject is entered into the study.

3.7 Cost to the subject

This retrospective case study has no costs to the subjects as the treatment has already been completed.

3.8 Withdrawal

Participation in the retrospective case study is voluntary and subjects may withdraw at any time by informing the study coordinator. An inquiry will be made as to the reason for termination.

4 Study protocol

4.1 Pre-treatment

Subjects underwent screening and baseline assessments (inclusion/exclusion criteria, physical examination) and examination of medical records. Eligible subjects were scheduled to return for the baseline visit and provided informed consent.

4.2 Baseline Data collection

Prior to scheduling, the subject's medical history and records were examined by the investigator. Once enrolled, clinical bloods (hematology) were conducted and SF-36 quality of life surveys were administered.

4.3 Procedure description

The procedure of this retrospective case study is to analyze the data and medical records of 13 subjects that were treated with allogeneic WJ-MSCs during the period from 2020 to 2021 at BHI Slovakia (Nemocnica Malacky hospital), Slovakia. To assess the safety of the study and to determine if the procedure exhibits a notable effect on targeted ailment or disease, the data of intake examinations, questionnaires and tests results will be collected and compared to the data of the same tests performed at specific stages of the therapy and post-therapy. Methods of descriptive statistics (significance is equal to 95%) and probability theory will be used. Analysis of results with the methods of descriptive statistics will be realized with the application of statistical software.

The therapy trial included the isolation of WJ-MSCs from the Wharton's Jelly fraction of umbilical cord tissue donated with consent of the mother following live birth at the maternity department in Malacky, Slovakia. The umbilical tissue was cleaned and placed in cultivation medium (79% DMEM (low glucose), 20% FBS, 1% Penicillin-Streptomycin) and incubated at 37°C, 5% CO_2, 90% humidity for 21 days. Cultivation medium was changed on day 7, 10 and 15. After 21 days, the cell culture was quality checked for blood cell cultivation and sterility. The WJ-MSCs were dissociated using trypsin and cryopreserved in 10% DMSO prior to treatment. WJ-MSCs were collected and processed under current good manufacturing practice (cGMP) and current good tissue practice (cGTP) specifications and follows a routine protocol across study sites. WJ-MSCS underwent initial pathogen testing for a range of infectious agents prior to cryopreservation or administration. Cell viability, identity and safety was confirmed following low-passage expansion.

Cultured WJ-MSCs were suspended in an infusion solution consisting of saline solution and the patient's own platelet rich plasma (PRP) for administration via intravenous, intrathecal or intraarticular infusion. A blood draw was collected from each subject and a serology analysis for the presence of HIV, Hepatitis B,C, Syphilis, CMV, and HTLV 1 , 2 performed. PRP was prepared

from each subject's blood draw.

For intravenous delivery in adults, 50mL of WJ-MSC infusion solution was administered consisting of 35 mL of saline solution, 10 mL patient's own PRP and 5 mL of cultured WJ-MSCs suspension. WJ-MSCs were filtered through a 170-260 micron filter to remove clots and infusion maintained at a rate of 100 milliliters per hour. For IV delivery only, 1 x 108 cell dosage is administered.

For intrathecal administration in adults, 2.5 mL of WJ-MSC infusion solution was administered consisting of 1.0 mL patients own PRP and 1.5 mL WJ-MSC suspension. Subjects were placed in the lateral position and a board-certified anesthesiologist sterilized the lumbar area prior to injection of 2% lidocaine for anesthesia. A spinal needle was inserted under sterile technique into the spinal canal and 2.5mL of cerebral spinal fluid was aspirated, and the volume replaced with the corresponding infusion of WJ-MSCs. For IV and intrathecal delivery, 7.5×10^7 cells are administered intravenously, and 2.5×10^7 cells are delivered by intrathecal injection (total cell dosage by both delivery routes is 1×10^8 cells). Where intrathecal administration was not tolerated by the subject, 1×10^8 cells was administered by IV infusion following pretreatment with Mannitol. At minute zero 25% mannitol was introduced into 100 cc of saline solution. The Mannitol solution was infused by intravenous injection over a 10- to 15-minute timeframe, followed immediately by IV infusion of WJ-MSCs as described above.

4.4 Follow up and End points

Subjects were tracked for 1 year to assess safety of WJMSC therapy and to evaluate effect on each patient-specific ailment. Outcome measurements in the form of laboratory blood test and SF-36 questionnaire scoring were completed approximately 6 months post-treatment. At 12 months post treatment, questionnaires and tests (laboratory blood tests and SF-36 questionnaires) will be administered to assess overall safety of WJMSC therapy and effect on various diseases or ailments.

4.5 Adverse reactions management and management

Adverse reactions were monitored immediately post-treatment and at six-month follow-up outcome measurements. No severe treatment related adverse events were reported post-treatment.

4.6 Data storing

Patient records will be maintained on a secure, password-protected server by authorized staff under the direction of BHI Therapeutic Sciences management. Insecure situations will be avoided. HIPAA compliant back-up data will be used. Patient data will be transmitted only as encrypted files. Information will not be released without the written permission of the participant, except as necessary for monitoring by IRB, the FDA, or the OHRP.

5 References

1. Mareschi K, Ferrero I, Rustichelli D, et al. Expansion of mesenchymal stem cells isolated from pediatric and adult donor bone marrow. *J Cell Biochem*. 2006;97(4):744-754. doi:10.1002/jcb.20681

2. Erices A, Conget P, Minguell JJ. Mesenchymal progenitor cells in human umbilical cord blood. *Br J Haematol*. 2000;109(1):235-242. doi:10.1046/j.1365-2141.2000.01986.x

3. Lee RH, Kim B, Choi I, et al. Characterization and expression analysis of mesenchymal stem cells from human bone marrow and adipose tissue. *Cell Physiol Biochem Int J Exp Cell Physiol Biochem Pharmacol*. 2004;14(4-6):311-324. doi:10.1159/000080341

4. Wang HS, Hung SC, Peng ST, et al. Mesenchymal stem cells in the Wharton's jelly of the human umbilical cord. *Stem Cells Dayt Ohio*. 2004;22(7):1330-1337. doi:10.1634/stemcells.2004-0013

5. Chapel A, Bertho JM, Bensidhoum M, et al. Mesenchymal stem cells home to injured tissues when co-infused with hematopoietic cells to treat a radiation-induced multi-organ failure syndrome. *J Gene Med*. 2003;5(12):1028-1038. doi:10.1002/jgm.452

6. Rustad KC, Gurtner GC. Mesenchymal Stem Cells Home to Sites of Injury and Inflammation. *Adv Wound Care*. 2012;1(4):147-152. doi:10.1089/wound.2011.0314

7. Bartholomew A, Sturgeon C, Siatskas M, et al. Mesenchymal stem cells suppress lymphocyte proliferation in vitro and prolong skin graft survival in vivo. *Exp Hematol*. 2002;30(1):42-48. doi:10.1016/s0301-472x(01)00769-x

8. Tyndall A, Walker UA, Cope A, et al. Immunomodulatory properties of mesenchymal stem cells: a review based on an interdisciplinary meeting held at the Kennedy Institute of Rheumatology Division, London, UK, 31 October 2005. *Arthritis Res Ther*. 2007;9(1):301. doi:10.1186/ar2103

9. Mukai T, Tojo A, Nagamura-Inoue T. Umbilical Cord-Derived Mesenchymal Stromal Cells Contribute to Neuroprotection in Neonatal Cortical Neurons Damaged by Oxygen-Glucose Deprivation. *Front Neurol*. 2018;9:466. doi:10.3389/fneur.2018.00466

10. Kinnaird T, Stabile E, Burnett M s., et al. Marrow-Derived Stromal Cells Express Genes Encoding a Broad Spectrum of Arteriogenic Cytokines and Promote In Vitro and In Vivo Arteriogenesis Through Paracrine Mechanisms. *Circ Res*. 2004;94(5):678-685. doi:10.1161/01.RES.0000118601.37875.AC

11. Sémont A, François S, Mouiseddine M, et al. Mesenchymal Stem Cells Increase Self-Renewal of Small Intestinal Epithelium and Accelerate Structural Recovery after Radiation Injury. In: Fisher JP, ed. *Tissue Engineering*. Advances in Experimental Medicine and Biology. Springer US; 2007:19-30. doi:10.1007/978-0-387-34133-0_2

12. Mosca JD, Hendricks JK, Buyaner D, et al. Mesenchymal stem cells as vehicles for gene delivery. *Clin Orthop*. 2000;(379 Suppl):S71-90. doi:10.1097/00003086-200010001-00011

13. Gao J, Dennis JE, Muzic RF, Lundberg M, Caplan AI. The dynamic in vivo distribution of bone marrow-derived mesenchymal stem cells after infusion. *Cells Tissues Organs*. 2001;169(1):12-20. doi:10.1159/000047856

14. Allers C, Sierralta WD, Neubauer S, Rivera F, Minguell JJ, Conget PA. Dynamic of distribution of human bone marrow-derived mesenchymal stem cells after transplantation into adult unconditioned mice. *Transplantation*. 2004;78(4):503-508. doi:10.1097/01.tp.0000128334.93343.b3

15. Liechty KW, MacKenzie TC, Shaaban AF, et al. Human mesenchymal stem cells engraft and demonstrate site-specific differentiation after in utero transplantation in sheep. *Nat Med*. 2000;6(11):1282-1286. doi:10.1038/81395

16. Devine SM, Bartholomew AM, Mahmud N, et al. Mesenchymal stem cells are capable of homing to the bone marrow of non-human primates following systemic infusion. *Exp Hematol*. 2001;29(2):244-255. doi:10.1016/s0301-472x(00)00635-4

17. Devine SM, Cobbs C, Jennings M, Bartholomew A, Hoffman R. Mesenchymal stem cells distribute to a wide range of tissues following systemic infusion into nonhuman primates. *Blood*. 2003;101(8):2999-3001. doi:10.1182/blood-2002-06-1830

18. Lalu MM, McIntyre L, Pugliese C, et al. Safety of Cell Therapy with Mesenchymal Stromal Cells (SafeCell): A Systematic Review and Meta-Analysis of Clinical Trials. *PLOS ONE*. 2012;7(10):e47559. doi:10.1371/journal.pone.0047559

19. Bang OY, Lee JS, Lee PH, Lee G. Autologous mesenchymal stem cell transplantation in stroke patients. *Ann Neurol*. 2005;57(6):874-882. doi:10.1002/ana.20501

20. Suárez-Monteagudo C, Hernández-Ramírez P, Álvarez-González L, et al. Autologous bone marrow stem cell neurotransplantation in stroke patients. An open study. *Restor Neurol Neurosci*. 2009;27(3):151-161. doi:10.3233/RNN-2009-0483

21. Barczewska M, Grudniak M, Maksymowicz S, et al. Safety of intrathecal injection of Wharton's jelly-derived mesenchymal stem cells in amyotrophic lateral sclerosis therapy. *Neural Regen Res*. 2019;14(2):313-318. doi:10.4103/1673-5374.243723

22. Pan K, Deng L, Chen P, et al. Safety and Feasibility of Repeated Intrathecal Allogeneic Bone Marrow-Derived Mesenchymal Stromal Cells in Patients with Neurological Diseases. *Stem Cells Int*. 2019;2019:e8421281. doi:10.1155/2019/8421281

23. Jaillard A, Hommel M, Moisan A, et al. Autologous Mesenchymal Stem Cells Improve Motor Recovery in Subacute Ischemic Stroke: a Randomized Clinical Trial. *Transl Stroke Res*. 2020;11(5):910-923. doi:10.1007/s12975-020-00787-z

24. Albu S, Kumru H, Coll R, et al. Clinical effects of intrathecal administration of expanded Wharton jelly mesenchymal stromal cells in patients with chronic complete spinal cord injury: a randomized controlled study. *Cytotherapy*. 2021;23(2):146-156. doi:10.1016/j.jcyt.2020.08.008

25. Lee JS, Hong JM, Moon GJ, Lee PH, Ahn YH, Bang OY. A Long-Term Follow-Up Study of Intravenous Autologous Mesenchymal Stem Cell Transplantation in Patients With Ischemic Stroke. *STEM CELLS*. 2010;28(6):1099-1106. doi:10.1002/stem.430

26. Mehling B, Hric M, Salatkova A, et al. A Retrospective Study of Stromal Vascular Fraction Cell Therapy for Osteoarthritis. *J Clin Med Res*. 2020;12(11):747-751. doi:10.14740/jocmr4354

27. Mehling B, Wu D, Quartararo L, et al. Allogeneic umbilical cord blood mononuclear cell therapy for spinal cord injury – a retrospective cohort study. Published 2018. Accessed July 29, 2021. https://www.semanticscholar.org/paper/Allogeneic-umbilical-cord-blood-mononuclear-cell-%E2%80%93-Mehling-Wu/ec8ea060097fd36591d4c39be623b2f81b002bf1

28. Jiang PC, Xiong WP, Wang G, et al. A clinical trial report of autologous bone marrow-derived mesenchymal stem cell transplantation in patients with spinal cord injury. *Exp Ther Med*. 2013;6(1):140-146. doi:10.3892/etm.2013.1083

29. Mehling BM. Evaluation of Immune response to Intravenously Administered Human Cord Blood Stem Cells in the Treatment of Symptoms Related to Chronic Inflammation. *J Stem Cell Res Ther*. 2015;05(08). doi:10.4172/2157-7633.1000297

30. Mehling BM, Quartararo L, Manvelyan M, Wang P, Wu DC. Safety Study of Intravenously Administered Human Cord Blood Stem Cells in the Treatment of Symptoms Related to Chronic Inflammation. *Int J Med Health Sci*. 2015;9(7):573-576.

31. Jin HJ, Bae YK, Kim M, et al. Comparative analysis of human mesenchymal stem cells from bone marrow, adipose tissue, and umbilical cord blood as sources of cell therapy. *Int J Mol Sci*. 2013;14(9):17986-18001. doi:10.3390/ijms140917986

32. Saleh M, Vaezi AA, Aliannejad R, et al. Cell therapy in patients with COVID-19 using Wharton's jelly mesenchymal stem cells: a phase 1 clinical trial. *Stem Cell Res Ther*. 2021;12(1):410. doi:10.1186/s13287-021-02483-7

33. Soder RP, Dawn B, Weiss ML, et al. A Phase I Study to Evaluate Two Doses of Wharton's Jelly-Derived Mesenchymal Stromal Cells for the Treatment of De Novo High-Risk or Steroid-Refractory Acute Graft Versus Host Disease. *Stem Cell Rev Rep*. 2020;16(5):979-991. doi:10.1007/s12015-020-10015-8

34. Hu J, Wang Y, Gong H, et al. Long term effect and safety of Wharton's jelly-derived mesenchymal stem cells on type 2 diabetes. *Exp Ther Med*. 2016;12(3):1857-1866. doi:10.3892/etm.2016.3544

35. Wang Y, Han ZB, Ma J, et al. A Toxicity Study of Multiple-Administration Human Umbilical Cord Mesenchymal Stem Cells in Cynomolgus Monkeys. https://home.liebertpub.com/scd. doi:10.1089/scd.2011.0441