Official Study Title:	SINGLE DONOR BANKED BONE MARROW MESENCHYMAL STROMAL CELLS FOR THE TREATMENT OF COVID-19 INDUCED ARDS: A NON-BLINDED RANDOMIZED, CONTROLLED STUDY (MSC FOR COVID-19)
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H-47561- SINGLE DONOR BANKED BONE MARROW MESENCHYMAL STROMAL CELLS FOR THE TREATMENT OF COVID-19 INDUCED ARDS: A NON-BLINDED RANDOMIZED, CONTROLLED STUDY (MSC FOR COVID-19)

Concise and Focused Presentation

We are asking you to take part in a research study to treat severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is caused by Coronavirus disease 2019 (COVID-19).

We want to see if specially designed immune cells called Mesenchymal Stromal Cells (MSCs) made from healthy individuals can help treat respiratory infections.

This study will be done in 2 parts. Your doctor will tell you which part of the study is open for enrollment. In the first part of the study, 6 subjects will receive treatment with MSCs (study drug). The first part of the study is called the 'safety run-in' phase. During the safety run in phase of the study all patients will receive the MSCs. In the second part of the study, 60 patients will be randomly assigned to group A (study drug + standard of care) or group B (standard of care).

If you are randomized to group A you will received MSCs and the standard treatment for your respiratory infection. If you are randomized to group B, you will only receive the standard treatment for your respiratory infection (so you will not receive Mesenchymal Stromal Cells (MSCs)). Standard treatment for your respiratory infection may include, but not limited to, the use of medications approved under the emergency use authorization such as remdesivir, anti-inflammatory antibodies and/or convalescent plasma.

If you take part in the study, you will have blood drawn to find out how you respond to the treatment. The study will last 28 days after your infusion of MSCs. You will be followed every day while you are hospitalized, and then weekly at weeks 2, 3, and 4 if discharged. Your doctors will follow you after your infusions either via telephone follow-up or with clinic visits if indicated.

Possible risks:
- Infusion reactions, though uncommon, have been reported in patients treated with MSCs, and consisted of symptoms such as fever, decrease in blood pressure, and decrease in the levels of oxygen in the blood.
- Since the person who provided the MSCs is not related to you, there is a possible risk that these "mismatched" MSCs will be rejected by your immune system. Rejection could cause you to become ill, with symptoms ranging from mild fever and rash, to more severe symptoms such as low blood pressure.
- A loss of confidentiality.
- We may not know all the risks.

Background

You are invited to take part in a research study. Please read this information and feel free to ask any questions before you agree to take part in the study.

You have a respiratory infection caused by COVID-19 that is not getting better. We want to give you mesenchymal stem cells (MSCs) from a healthy donor to see if the cells will help your immune system fight the infection.

To test if treatment with MSCs is better than the standard treatment for COVID-19 related respiratory infection, you will be randomly assigned to Group A (study drug) or Group B (control).

Stem cells are cells that do not yet have a specific function in the body. Mesenchymal stem cells (MSCs) are a type of stem cell that can be grown from bone marrow (the spongy tissue inside of bones). Stem cells can develop into other types of more mature (specific) cells, such as blood and muscle cells.

For this treatment we will use MSCs from a healthy donor to give to you. The MSCs are considered an investigational treatment not approved by the Food and Drug Administration (FDA) for this treatment. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Purpose
This study will be done in 2 parts.

The purpose of the first part of this study is to see if there are any unexpected side effects.

The purpose of the second part of this study is to compare treatment with MSCs for the treatment of respiratory infections caused by COVID-19 to routine hospital care for patients.

Procedures
The research will be conducted at the following location(s):
Baylor College of Medicine and TMH: The Methodist Hospital.

Approximately 66 subjects may be treated on this study.

This study will be done in 2 parts. Your doctor will tell you which part of the study is open for enrollment. In the first part of the study, 6 subjects will receive treatment with MSCs (study drug). The first part of the study is called the 'safety run-in' phase. In the second part of the study, 60 patients will be randomly assigned to group A (study drug) or group B (control).

Randomization
You will be randomly assigned to a study group. We'll use a computer to put you into study group A (study drug) or group B (control) by chance (randomized). You have an equal chance of getting the study drug or placebo. It's just like flipping a coin. If you're randomized to the control group, you will get the standard treatment for your respiratory infection.

You or your doctor will not choose your group. Once you're assigned a group, you or your doctor can not change your group.

Group A Treatment

Prior to the treatment we will do a SARS-CoV-2 test, conduct a physical exam, collect blood for laboratory work, obtain a chest X-ray or chest CT Scan (if one was not already done as part of your clinical care) and do a pregnancy test (for females). These tests are done to assess your eligibility to receive the cells.

On the day you are scheduled to receive the cells you will be pre- medicated with Benadryl and Tylenol. You will then receive a single intravenous (into the vein) infusion of MSCs. You will be monitored closely for two hours after the infusion. After that your care will be standard for your condition. If after 3-5 days your condition does not get better, you may receive another infusion of MSCs.

As part of the research study we will be evaluating you daily for 7 days and then weekly at weeks 2, 3, and 4. These evaluations will include a physical exam and blood collection at each time point unless you are discharged.

A chest X-ray or chest CT scan will be done on days 1, 3, 5, 7, week 2, week 3, and week 4 (if not done as part of your clinical care).

To learn more about how COVID-19 affects the immune system, extra blood will be drawn. The total amount on any day will be ~ 4 tablespoons (~50 mL). Blood will be taken prior to the infusion of the MSCs, at day 1, 3, 5, 7, 14, and at day 28 if you are still hospitalized. The total blood drawn for research during your participation in this study will not exceed 200 mL (~16 tablespoons).

If you decide to withdraw at any time during the study both samples and data collected during your participation will be maintained.

The remaining blood and/or tissue samples that are not needed directly for you could be used to help researchers learn about this disease. The specimens will be kept until the samples are exhausted. These specimens and information about your circumstances may be shared with other cancer researchers or third party laboratories.

Samples will be kept at Baylor College of Medicine indefinitely. Although there will be a record identifying under what circumstances these specimens were obtained, under all circumstances your identity will be kept confidential. There is a small risk for the loss of confidentiality. However, study personnel will make every effort to minimize this risk.

Group B Treatment

If you are assigned to Group B, you will receive supportive care or treatment designated by your treating doctor. This may include, but not limited to, the use of medications approved under the emergency use authorization such as remdesivir, anti-inflammatory antibodies and/or convalescent plasma. You will not

receive Mesenchymal stem cells.

Subjects on assigned to group B will undergo the same blood sample collections as those in group A for comparison purposes. Chest imaging will be done per standard of care, but data from the medical record will be collected at the same timepoints as group A if available

Clinically Relevant Research Results

The results generated from this research study are not expected to have any clinical relevance to you.

Sharing and Future Research Studies with Identifiable Private Information

Information that identifies you may be removed from your identifiable private information collected as part of this research, and after such removal, your information may be used for future research studies or distributed to another investigator for future research studies without additional consent/authorization from you.

Sharing and Future Research Studies with Identifiable Biospecimens

Information that identifies you may be removed from your identifiable biospecimens collected as part of this research, and after such removal, your biospecimens may be used for future research studies or distributed to another investigator for future research studies without additional consent/authorization from you.

Research related health information

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you sign this document, you give permission to people who give medical care and ensure quality from Baylor College of Medicine and TMH: The Methodist Hospital to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes:

- Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
- Demographic information (name, D.O.B., age, gender, race, etc.)
- Billing or financial records

The health information listed above may be used by and or disclosed (released) to researchers, their staff and their collaborators on this research project, the Institutional Review Board, Baylor College of Medicine, and TMH: The Methodist Hospital.

Agents of the U.S. Food and Drug Administration may inspect the research records including your health information. Agents of regulatory agencies such as the U.S. Department of Health and Human Services will be permitted to inspect the research records including your health information.

A Data and Safety Monitoring Board will have access to the research records including your health information.

Use or Disclosure Required by Law

Your health information will be used or disclosed when required by law.

Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability and conducting public health surveillance, investigations or interventions.

Baylor College of Medicine and TMH: The Methodist Hospital are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine and TMH: The Methodist Hospital to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

Please note that the research involves treatment. You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment. To maintain the integrity of this research study, you generally will not have access to your personal health information related to this research until the study is complete. However, your health information that is necessary to your care will be provided to you or your physician. At the conclusion of the research and at your request, you generally will have access to your health information that Baylor College of Medicine and TMH: The Methodist Hospital maintain in a designated record set, which means a set of data that includes medical information or billing records used in whole or in part by your doctors or other health care providers at Baylor College of Medicine and TMH: The Methodist Hospital to make decisions about individuals. Access to your health information in a designated record set is described in the Notice of Privacy Practices provided to you by representatives of the specific institution where you are being enrolled into this research study which are: Baylor College of Medicine and TMH: The Methodist Hospital.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers, their staff and their collaborators on this research project, the Institutional Review Board, regulatory agencies such as the U.S. Department of Health and Human Services, FDA, Baylor College of Medicine, Data and Safety Monitoring Board, and TMH: The Methodist Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization.

To revoke this Authorization, you must write to: LaQuisa Hill, MD
Center for Cell and Gene Therapy
Houston Methodist Hospital

This authorization does not have an expiration date. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

Potential Risks and Discomforts

RISKS RELATED TO MSCs:

Infusion-Associated Reactions:

Infusion reactions, though uncommon, have been reported in patients treated with MSCs, and consisted of symptoms such as fever, decrease in blood pressure, and decrease in the levels of oxygen in the blood. To reduce the potential for infusion reaction, you will receive medication prior to administration of MSCs. In addition, level of oxygen in the blood is monitored during infusion of the product.

POSSIBLE SIDE EFFECTS OF MSCs:

Patients receiving MSCs may have side effects involving almost every organ in the body . These side effects may not be due to MSCs but due to the disease or illness for which the MSCs are being used to treat.

COVID-19 disease is associated with abnormal blood clotting and an increased risk of developing blood clots (hypercoagulable state) during the course of the illness.

Treatment with MSCs may slightly increase the risk of developing a blood clot but is easily prevented with the use of low dose blood thinners (anticoagulation). Thus, blood thinners are given at low doses as standard of care to patients with COVID-19 disease to prevent the development of blood clots, which would also help prevent development of any blood clots from the MSC infusion. If you are not able to receive blood thinners, then you will not be eligible to receive the MSC infusion.

For patients with cancer, administration of MSCs could potentially increase the risk of relapse by reducing anti-tumor responses.

Long-term safety information of the use of MSCs is still unknown.

As with any investigational agent, there may be side- effects and discomforts that are not yet known.

You should be aware that a number of possible safety risks exist. These include the following:

Potential Contamination and Infection:

This product is made from human bone marrow. As such, it is possible that any viruses in the blood of the person who donated the bone marrow could still be present in the treatment given to you. This risk is considered to be extremely low due to the extensive screening and testing of the marrow donors, and testing of the final MSC product.

Possible Immune Reaction (including rashes and joint aches):

Since the person who provided the MSCs is not related to you, there is a possible risk that these "mismatched" donor MSCs will be rejected by your immune system. If rejection occurs, the donor MSCs will not survive in your body. Rejection may not cause any symptoms, but it is possible that rejection could cause you to become ill, with symptoms ranging from mild fever and rash, to more severe symptoms such as low blood pressure.

In rare circumstances, it is possible that an allergic reaction to the investigational agent may occur. An allergic reaction could result in hives, rash, difficulty breathing, low blood pressure, or severe blood circulation and breathing problems. These reactions are usually reversible, but in rare cases could lead to permanent disability or death. You will receive pre-medication to help prevent an allergic reaction.

Potential Adverse (Bad) Effects with Dimethyl Sulfoxide (DMSO):

In order to appropriately store MSCs, it must be frozen. DMSO is a chemical substance used to help freeze the MSCs. In some animal studies, DMSO has been reported to have possible adverse effects on the heart, and DMSO has been reported to decrease heart rates in patients. DMSO has also been associated with potential allergic reactions. You may experience no side-effects, but you could experience mild ones, such as an unusual "garlic" taste in his mouth, nausea, skin flushing, coughing, shortness of breath, or chest tightness.

Risk of Ectopic Tissue Formation:

Ectopic tissue formation is the formation of tissue in areas of the body it would not normally be found. Human MSCs cultured in the laboratory possess the ability to become other types of tissues, such as bone and cartilage, under appropriate conditions. More than 500 subjects have been treated with MSCs, and only one case of ectopic tissue formation has been reported.

POSSIBLE SIDE EFFECTS OF THE PREMEDICATIONS:
The primary side effect of the pre-medications is drowsiness.

POSSIBLE SIDE EFFECTS OF CHEST X-RAYS AND CHEST CT SCANS

The use of excessive chest X-rays and CT scans has been linked to cancer. You may not have additional chest X-rays or CT scans while you are on this study as they may be needed to monitor your clinical condition however if you do receive additional X- rays or CT scans we do not consider that to be a significant risk during this short study.

Because of potential or unknown effects of the study on a fetus, if you are a woman of child-bearing potential, you must have a negative serum pregnancy test prior to entry into this study.

You have been informed that either you or your partner(s) must utilize one of the more effective birth control methods during the study and for six months after the study is concluded. These consist of total abstinence, oral contraceptives, an intrauterine device and, contraceptive implants under the skin or contraceptive injections. If one of these methods cannot be used, contraceptive foam with a condom is allowed. In addition, the male partner should use a condom.

There may be unknown risks or discomforts involved. Study staff will update you in a timely way on any new information that may affect your decision to stay in the study. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

Potential Benefits

The benefits of participating in this study may be: infusing these MSCs may help your immune system fight SARS-CoV-2 and help you recover from the infection. We do not know if that will happen. Some information from your treatment may help us learn more about MSCs and help other patients in the future. However, you may receive no benefit from participating.

Alternatives

The following alternative procedures or treatments are available if you choose not to participate in this study: Receive a different investigational treatment or continue current treatments.

Current standard of care therapies for hospitalized patients requiring high-flow nasal cannula (HFNC) oxygenation, Noninvasive positive pressure ventilation (NIV), or mechanical ventilation (MV) are: Remdesivir with dexamethasone + baricitinib (tofacitinib may be used as an alternative if baricitinib unavailable) OR dexamethasone + tocilizumab (sarilumab may be used as an alternative if tocilizumab unavailable). Please refer to NIH COVID-19 Treatment guidelines https://www.covid19treatmentguidelines.nih.gov/

Patients on either arm of the study may receive these therapies as standard of care treatment. Patients randomized to the MSC arm would get standard of care treatment as deemed appropriate by the treating team, in addition to receiving mesenchymal stromal cells (MSCs). Patients on the standard of care treatment only arm would receive standard therapies per the discretion of the treating physician.

Investigator Withdrawal of Subject from a Study

The investigator or sponsor may decide to stop you from taking part in this study at any time. You could be removed from the study for reasons related only to you (for example, if you move to another city, if you do not take your study medication, or if you have a serious reaction to your study medication) or because the entire study is stopped. The sponsor, investigator, Food and Drug Administration, or Institutional Review Board may stop the study at any time.

Subject Costs and Payments

You will not be charged for the preparation or manufacture of the Mesenchymal Stromal cells , nor will you be charged for the laboratory studies done to monitor the how well these cells are working and to measure how long they stay in your body. You and/or your insurance company may be charged for some research related costs including the infusion of the cells. You and/or your insurance company will be responsible for medical services provided that are part of the standard of care for your infection (including some supportive care treatments, laboratory, and disease evaluations). Financial counseling is available if needed.

You will not be paid for taking part in this study.

This institution may use your biospecimens (even if identifiers are removed) for commercial profit, however, the institution does not plan to pay royalties (share with you in the commercial profit) to you if a commercial product is developed from any biospecimens (blood or tissue) obtained from you during this study.

Research Related Injury

If you are injured as part of your participation in this study, there are no plans to pay you.

Research personnel will try to reduce, control, and treat any complications from this research. If you are injured because of this study, you will receive medical care that you or your insurance will have to pay for just like any other medical care.

Subject's Rights

Your signature on this consent form means that you have received the information about this study and that you agree to volunteer for this research study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these benefits, services, or rights.

The investigator, LAQUISA HILL, and/or someone he/she appoints in his/her place will try to answer all

of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: LAQUISA HILL at (713) 441-1450 during the day and after hours.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research, if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.

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Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Subject	Date
Legally Authorized Representative - Adult	Date
Investigator or Designee Obtaining Consent	Date
Witness (if applicable)	Date
Translator (if applicable)	Date