INFORMED CONSENT FORM

IND 27536

HBPD04

"A Randomized, Double-Blind, Single Center, Phase 2, Efficacy and Safety Study of allogeneic HB-adMSCs vs Placebo for the Treatment of Patients with Parkinson's Disease"

NCT04995081

Document Date: August 31, 2022

IRB APPROVED
AS MODIFIED
Aug 31, 2022

INFORMED CONSENT FORM TO TAKE PART IN A RESEARCH STUDY

TITLE:	A Randomized, Double-Blind, Single Center, Phase 2, Efficacy and Safety Study of allogeneic HB-adMSCs vs Placebo for the Treatment of Patients with Parkinson's Disease
PROTOCOL NO.:	HBPD04 WCG IRB Protocol #20213071
STUDY TREATMENTS:	HB-adMSCs (allogeneic) Placebo
SPONSOR:	Hope Biosciences Stem Cell Research Foundation
INVESTIGATOR:	Djamchid Lotfi, MD 16700 Creek Bend Dr. Sugar Land, TX 77478
EMERGENCY CONTACT:	Sherry Diers, RN 16700 Creek Bend Dr Sugar Land, TX 77478
STUDY-RELATED PHONE NUMBER(S):	Djamchid Lotfi, MD Telephone: 346 900 0340 (24 hours) Email: lotfi99@yahoo.com Sherry Diers, RN Telephone: 346 900 0340 Ext 101 Email: sherry@hopebio.org

DocuSigned by:
DLM
Signer Name: Djamchid Lotfi MD
Signing Reason: I approve this doc
Signing Time: 9/14/2022 | 8:48:54 A
8BFDB82AA7CB47F498D963BFE

This informed consent form to be used in this clinical trial is divided into two sections as described below,

1. General information about volunteering participation in this research study.
2. Certificate of Consent by Study Participant and Principal Investigator or Delegated Staff.

SECTION 1: INFORMATION SHEET.

You are invited to participate in this research study since you have been diagnosed with mild to moderate Parkinson's disease. This document also known as the Informed Consent Form will include the following basic elements that will allow you to decide your voluntary participation in this research study:

- Description of the clinical investigation. Including purposes of the research study, expected duration and description of the procedures.
- Risks and Discomforts. This includes risks and discomforts of tests, intervention and procedures required by protocol.
- Benefits. A description of any benefits to the study participant or to others which may be reasonably be expected from this research study.
- Alternative Procedures or Treatments. This includes alternative procedures or treatments that might be beneficial to the study participant.
- Confidentiality of the information collected during participation in the study.
- Compensation and Medical Treatment in Event of Injury.
- Contacts for answers to research study questions and research subject's rights.
- Voluntary participation. This includes a statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits.
- Other elements, such as the involuntary termination of the subject's participation and the number of subjects, etc.

When reading the informed consent form there may be some words that you do not understand. If so, please ask the principal investigator and/or study coordinators about it and they will take time to explain.

1.1 Description of the Clinical Investigation.

Parkinson's disease is considered the second most prevalent and incidental neurodegenerative disorder, affecting more than 2% of the population older than 65 years old. This disease causes not only dysfunction of movement but also an extensive range of motor symptoms. Although the cause of Parkinson's disease remains unclear, the risk of developing this disease is no longer viewed as primarily due to environmental factors. Instead, Parkinson's disease seems to result from a complicated interplay of genetic and environmental factors affecting numerous fundamental cellular processes. The complexity of Parkinson's disease is accompanied by

clinical challenges, including an inability to make a definitive diagnosis at the initial stages of the disease and difficulties in the management of symptoms at later stages.

Current treatments of Parkinson's disease include Levodopa, direct agonist of the dopaminergic receptors and anticholinergic agents. Levodopa was approved to treat Parkinson's disease over 50 years ago and although considered a first-line treatment, this drug has major complications that may arise in up to 80% of cases. Some of these complications are:

- The response to the medication may wear off (going from four to six hours when the drug is first administered to one to two hours for the same dosage).
- The appearance of dyskinesia. (abnormality or impairment of voluntary movement) Dyskinesias in long term levodopa therapy are not well understood and hard to manage. New disabilities can develop that are less responsive to levodopa even with increased doses and can often lead to toxicity.

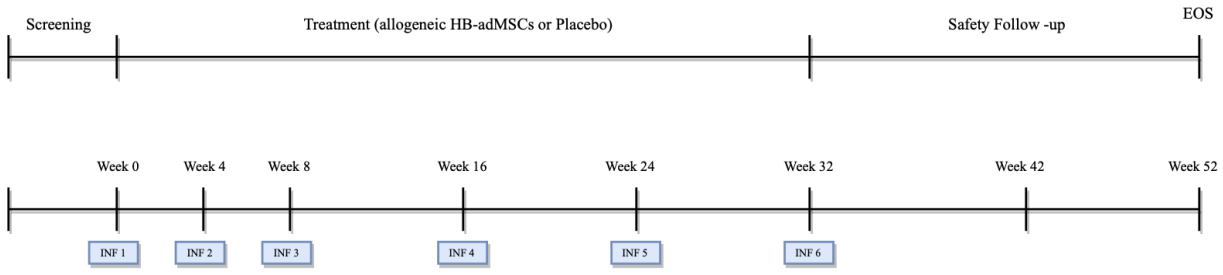
Other potential treatments for this disease could be investigated using clinical trials, also known as clinical studies, where safety and efficacy of research products are investigated to see whether they should be approved for wider use in the general population.

Hope Biosciences allogeneic adipose derived mesenchymal stem cells (HB-adMSCs) is an Investigational Drug- Limited by Federal law to investigational use. Adipose refers to fat cells and allogeneic refers to cells coming from a screened donor. The purpose of this research study is to evaluate the safety and effectiveness of this investigational drug. The investigational product has been tested in animals and used in other human trials.

1.2 Type of Research Intervention

If you agree to participate in this research study, you will have 9 study visits over a period of 52 weeks approximately. See study visits below.

Figure 1 Schedule of the visits.



1.3 Selection of Study participants

A total of 60 patients with mild to moderate Parkinson's Disease patients will be evaluated at screening. The screening period can take up to 28 days. Once screened and if found eligible, subjects are randomized (assigned by chance) to receive either Allogeneic HB-adMSCs or placebo. A placebo is an inactive substance. Randomized means neither you nor your study doctor can decide the group to which you are assigned. Thirty subjects will be randomly assigned to the placebo group. Thirty subjects will be randomly placed in the treatment group. You will then be contacted to schedule the following study visits.

1.4 Voluntary participation

The participation of each patient in this research study is entirely voluntary. Whether a patient decides to participate or not, all the services provided to them at Hope Biosciences Stem Cell Research Foundation will remain the same and nothing will change. Although a patient has decided to participate, the decision to withdraw from the study can be made at any time. The decision, to participate or to withdraw participation, will not result in any penalty or loss of benefits to which you are otherwise entitled.

1.5 Information on the research drug

The research drug we are testing in this clinical investigation is called HB-adMSCs. This research drug is investigational, which means that it is not approved by the Food and Drug Administration (FDA). This research drug is manufactured by Hope Biosciences, LLC a biotechnology company.

1.6 Study procedures

If you agree to participate in this research study, the principal investigator or designated staff will perform the following procedures during your participation:

- Collection of Informed Consent before any study procedure begins.
- Collection of Medical History and current medications.
- Measurement of Height and Weight.
- Collection of Vital Signs including respiratory rate, pulse rate, blood pressure, body temperature and oxygen saturation.
- Collection of blood samples (approximately 15 ml, or one tablespoon of blood) from a vein of your arm using a needle to evaluate your health status and the effects of the investigational product, and also urine pregnancy tests if female of childbearing potential.
- You will need to complete patient questionnaires during some of the clinic visits.
- The principal investigator will conduct a physical exam to assess your health status prior to each administration of the investigational product.
- The investigational product or placebo will be given through a vein in your arm at visits 2, 3, 4, 5, 6 and 7 with monitoring of vital signs for an hour during and 1 hour after administration.

- 24 hours after the investigational product or placebo administration the principal investigator or designated staff will contact you through a phone call to evaluate the incidence of any reactions.

The following table includes the different procedures to perform for this research study, as well as the duration of it.

	Visit 1		Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10
Visit Names	**Screening**		**INF 1**	**INF 2**	**INF 3**	**INF 4**	**INF 5**	**INF 6**	**F/U**	**F/U**	**EOS**
Window Period	**Up to 28 days**		**± 7 days**	**± 7 days**	**± 7 days**	**± 7 days**	**± 7 days**	**± 7 days**	**± 7 days**	**± 7 days**	**± 7 days**
Visit Weeks	**N/A**		**0**	**4**	**8**	**12**	**16**	**20**	**24**	**42**	**52**
Informed Consent	•										
Demographics	•										
Medical History	•		•	•	•	•	•	•	•	•	•
Prior and Concomitant Medications	•		•	•	•	•	•	•	•	•	•
Eligibility Criteria	•		•								
Vital Signs	•		•	•	•	•	•	•	•	•	•
Weight	•		•	•	•	•	•	•	•	•	•
Height	•										
Laboratory Samples [1]	•		•				•			•	•
Physical Examination	•		•	•	•	•	•	•	•	•	•
Parkinson's Disease Assessments [2]	•		•	•	•	•	•	•	•	•	•
Dose of carbidopa/levodopa taken in the last 24 hours (if applicable)	•		•	•	•	•	•	•	•	•	•
Levodopa Equivalent Dose Calculation (if applicable)	•		•	•	•	•	•	•	•	•	•
Study Treatments Administration			•	•	•	•	•	•			
24 hours Telephone Encounter			•	•	•	•	•	•			
Video Documentation	•		•				•				•
AE and SAE assessments			•	•	•	•	•	•	•	•	•

Randomization

1. If the period of time between Visit 1 - Screening and Visit 2 – Infusion 1 (Baseline) is less than 10 days, the following assessments will not be required during Visit 2 – Infusion 1 (Baseline): Collection of laboratory samples (CBC, CMP & Coagulation Panel) and Video documentation.
2. Parkinson's disease Assessments – MDS-UPDRS, VAS pain and muscle spasms, SF-36 Parkinson's disease fatigue scale (PFS-16) and Parkinson's disease Questionnaire (PDQ-39).

1.7 Side Effects

HB-adMSCs are considered a biologic drug under investigation, the administrations of this research drug may be associated with unwanted side effects, unknown risks, including possible worsening of your medical condition and a risk of life-threatening complications. If a study participant develops any of these risks, the study team will notify each participant in a timely manner.

If changes are made to the study, a new informed consent will be required. Study coordinators will be in contact with each active study participant if this event is present.

Possible side effects to monitor for infusion reactions are mentioned below:

- Low-grade fever
- High or low blood pressure
- Difficulty breathing
- Venous thromboembolic events

It is possible that it may also cause some side effects that we are not aware of. However, we will follow each study participant closely and keep track of any unwanted effects or any problems. Approved over the counter medicines, an analgesic, Aspirin 81 mg, and an antihistamine drug (either Loratadine 10 mg or Cetirizine Hydrochloride 10 mg) will be given by mouth before investigational product administration to treat any side effect or reactions. If indicated by Principal Investigator or regulatory agencies the use of the research drug may be stopped.

1.8 Risks

1.8.1 General Risks

By participating in this research study, it is possible that you will be at greater risk than you would otherwise be. There is, for example, a risk that your Parkinson’s disease will not get better and that the investigational product doesn't work, or your condition could get worse.

1.8.2 Blood Draw

Obtaining blood samples may cause minor discomfort, feeling lightheaded, fainting, bruising, clotting, bleeding from the site of blood collection and in rare cases infection.

1.8.3 Intravenous Injections

- Occasionally: Slight discomfort, bruising, and pain on the site of injection.

- Rarely: Inflammation of the area of injection, phlebitis (inflammation in vein), metabolic disturbances, catheter or air embolism (air causing a blockage in blood vessels), venous puncture, irregular heartbeat, and venous thrombosis (blood clot in veins).

- Very rarely: Severe allergic reaction, anaphylaxis, infection, cardiac arrest, respiratory distress, pulmonary embolism (blood clot in lungs) and death.

1.8.4 Pregnancy/Birth Control

The effects of HB-adMSCs on human reproductive organs and unborn babies has not been studied and may be harmful in ways we do not currently know.

For Women: If you are pregnant, planning to become pregnant, or are breastfeeding a child, you cannot participate in this study.

For Women & Men: Female participants of childbearing potential and male participants who are sexually active with a woman of childbearing potential must agree to use at least 1 highly effective form of birth control throughout the study and for 6 months after the last dose of the investigational product. Highly effective methods of birth control include true sexual abstinence, bilateral tubal ligation, vasectomy, intrauterine device and hormonal contraceptive methods.

1.8. 5 Risks of Other Drugs Used in the Study

Prior to each study infusion, you will be given Aspirin 81 mg, and an antihistamine drug.

The risks of aspirin include: an allergic reaction and the possibility that it could make you bruise or bleed.

The risks of the antihistamine mainly include drowsiness, dizziness. dry mouth, visual changes, difficulty urinating, and constipation.

1.9 Benefits

The benefits of this investigational product in patients with PD is unknown. There are FDA-approved treatments for PD. (see below Alternatives sec. 1.10)

There may not be any benefit for study participants, but their participation may help us find the answer to the research question. There may not be any benefit to the society at this stage of the research, but future generations may benefit.

1.10 Alternatives

The conventional pharmacological approved by FDA are listed below:

Generic Name	Trade Name
Carbidopa-levodopa	Sinemet
Carbidopa-levodopa (controlled release)	Sinemet CR
Carbidopa-levodopa (orally disintegrating tablet)	Parcopa
Carbidopa-levodopa (extended release capsules	Rytary
Carbidopa-levodopa-entacapone (enteral suspension)	Duopa
Levodopa Inhalation powder	Inbrija
Entacapone	Comtan
Tolcapone	Tasmar
Opicapone	Ongentys
Carbidopa/Levodopa Entacapone	Stalevo
Pramipexole	Mirapex
Pramipexole (extended release)	Mirapex ER
Ropinirole	Requip
Ropinirole (extended release)	Requip XL
Apomorphine (injection)	Apokyn
Apomorphine sublingual film	Kynmobi
Rotigotine (transdermal patch)	Neupro
Selegiline	Eldepryl
Selegiline (orally disintegrating tablet)	Zelapar
Rasagiline	Azilect
Safinamide	Xadago
Amantadine	Symmetrel
Amantadine (extended release)	Gocovri
Amantadine (extended release)	Osmolex

Istradefylline	Nourianz
Trihexyphenidyl	Artane
Benztropine	Cogentin

There are also surgical treatments and other strategies currently being explored in the treatment of some Parkinson's disease symptoms. Some of these strategies are, lifestyle modifications, physical and speech therapy.

1.11 Costs and Reimbursements

The study sponsor (Hope Biosciences Stem Cell Research Foundation) will pay for all study related visits and procedures.

If a participant receives a bill that is related to this research study, the principal investigator Djamchid Lotfi MD should be contacted at (346) 900 0340 or the study coordinator at (346) 900-0340 Ext. 101.

You will not be paid for being in this study.

1.12 Confidentiality

The information that we collect from this research study will be kept confidential. Information about study participants that will be collected will be kept safe and no one but the researchers and the individuals and organizations listed below will be able to see it. Any information about study participants will have a number on it instead of a name. However, absolute confidentiality cannot be guaranteed.

Private information and medical record will be shared with individuals and organizations that conduct or watch over this research, including:

- The research sponsors
- People who work with the research sponsor
- Government agencies, such as the Food and Drug Administration
- The Institutional Review Board (IRB) that reviewed this research

We may publish the results of this research. However, we will keep subject's name and other identifying information confidential.

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. This website is available to everybody.

1.13 Right to Refuse or Withdraw

At any time after signing informed consent, each study participant has the right to refuse and/or withdraw from participating in the research study and all the rights and benefits will be respected. Sponsor, Principal Investigator, Institutional Review Board and/or FDA have the right to stop study participation at any time. If the study is stopped, study participants shall be followed by principal investigator until end of the study or resolution of an adverse events/serious adverse event.

1.14 Who to Contact?

If any questions, concerns or complaints arise during study participation, the study subjects have the right to ask to the Principal Investigator, Djamchid Lotfi, MD at 346 900 0340 (24 hours) or lotfi99@yahoo.com, the emergency contact, Sherry Diers, RN at 346 900 0340 Ext 101 or sherry@hopebio.org, or WCG IRB. An IRB is a group of people who perform independent review of research studies. See contact information below:

Telephone: 855-818-2289,
Email: researchquestions@wcgirb.com

Some of the situations in which WCG IRB can be contacted are listed below:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

1.15 Injuries related with study participation

If a study participant is injured or get sick because of being in this research, the principal investigator should be contacted immediately. The principal investigator will provide emergency medical treatment. Medical insurance may be billed for this treatment. The sponsor will pay any charges that are not covered by insurance policy or the government, provided the injury was not due to underlying illness or condition and was not caused by study participants or some other third party. No other payment is routinely available from the study doctor or sponsors.

IRB APPROVED
AS MODIFIED
Aug 31, 2022

IMPORTANT

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions. Signing your name to this consent form means that you voluntarily agree to take part in this study. This agreement can be withdrawn at any time.

SECTION 2: CERTIFICATE OF CONSENT.

2.1 Study's Participant

I've read the above information, and I am aware that I am being asked to participate in a research study. I have had the chance to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study. I have been informed that I may leave the study at any time without affecting my medical care and the Sponsor or my doctor may withdraw me from the study without my consent.

I understand that during the study I will have the following responsibilities:

- Attend all scheduled visits.
- Stay on my stable regimen of treatment.
- Follow the study doctor's instructions about whether I may continue to take my regular medications or other prescribed or over-the-counter medicines during the study period.
- Tell the study doctor of any changes to my current medications, illnesses or injuries, unexpected or troublesome side effects, or problems that occur during the study.
- Tell the study doctor if I plan to have an elective surgery or any other medical treatment or procedure.
- I should continue to make regular visits to my primary doctor or any other special doctors that I was seeing before starting the study. I understand that enrollment in this study does not replace regular medical care.
- Contact the study doctor if I have any questions about the study after I sign this form.

I authorize the release of my medical records to Hope Biosciences and its agents, the U.S. regulatory agency, FDA, and the Institutional Review Board.

I am not giving up any legal rights by signing this form. I will be given a copy of this form. I consent voluntarily to participate as a participant in this research.

_____	_____
Print Name of Study's Participant	Date
_____	_____
Signature of Study's Participant	Time

2.2 Statement by the researcher/person taking consent

I have carefully explained to the subject the nature of the study. I hereby certify that to the best of my knowledge the subject signing this consent form/authorization understands clearly the nature, demands, risks and benefits involved in participating in this study. A medical problem or language or educational barrier has not prevented a clear understanding of the subject's involvement in this study.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability.

I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

_____	_____
Print name of researcher/person taking consent	Date
_____	_____
Signature of researcher/person taking consent	Time