Clinical Trial Protocol
Iranian Registry of Clinical Trials

31 May 2026

Evaluating the Safety of Placenta Mesenchymal Stem Cells-derived Exosomes (HP-MSCs-derived Exosomes) in the Treatment of Steroid-Resistant Acute GVHD after Allogeneic Hematopoietic Stem Cell Transplantation: Clinical Trial Phase I

Protocol summary

Study aim

Exosome therapy with exosomes derived from mesenchymal stem cells in acute steroid-resistant transplant disease

Design

This trial is a single-arm phase 1-2 interventional study (non-randomized and non-blinded) for 12 patients, the aim of which is to investigate the safety of exosomes derived from placental mesenchymal stem cells in transplant disease against the acute steroid-resistant host.

Settings and conduct

This study is a single-group clinical trial to evaluate the safety of exosomes derived from placental mesenchymal stem cells in the laboratory for the treatment of transplant disease against acute steroid-resistant host in Taleghani Hospital of Shahid Beheshti University of Medical Sciences.

Participants/Inclusion and exclusion criteria

Inclusion: Grade II to IV acute Graft Versus Host Disease (aGVHD) patients, poor response to corticosteroids, signed written informed consent Exclusion: Recurrence of the main disease (cancer), use of Infliximab, Infections

Intervention groups

Routine treatment and injection of one unit of exosome derived from mesenchymal stem cells is almost equivalent to the number of exosome particles, which is 10 to the power of 11, prepared from every 10 to the power of 8 cells, which is done at the same rate in the recipient group weighing 50 to 80 kg.

Main outcome variables

Recurrence of acute Graft Versus Host Disease (aGVHD) and infection; Overall Remission Rate; Progression-free survival; Duration of Response

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20200413047063N6**
Registration date: **2025-05-24, 1404/03/03**
Registration timing: **registered_while_recruiting**

Last update: **2025-05-24, 1404/03/03**
Update count: **0**

Registration date

2025-05-24, 1404/03/03

Registrant information

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Recruitment status

recruiting

Funding source

Expected recruitment start date

2024-12-30, 1403/10/10

Expected recruitment end date

2026-12-31, 1405/10/10

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date
empty

Scientific title
Evaluating the Safety of Placenta Mesenchymal Stem Cells-derived Exosomes (HP-MSCs-derived Exosomes) in the Treatment of Steroid-Resistant Acute GVHD after Allogeneic Hematopoietic Stem Cell Transplantation: Clinical Trial Phase I

Public title
Exosome therapy in steroid-resistant acute Graft Versus Host Disease (GVHD) patients

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Patients diagnosed with grade II to IV acute Graft versus host disease (GVHD) whose response to treatment with corticosteroids equal to or more than 2 milligrams per kilogram is poor, and the disease symptoms progress in three days or have stable disease for five days Patients over 18 years old Patients of both sexes Signed written informed consent

Exclusion criteria:
Patients who have recurrence of the main disease (cancer) Patients who, in the differential diagnosis of clinical symptoms, have causes other than acute graft versus host disease (aGVHD) indicating the patient, such as patients with symptoms Sinusoidal Obstruction Syndrome (SOS), maculopapular skin rashes with drug or viral causes or Engraftment Syndrome, viral diarrheas, etc Patients who have been prescribed Infliximab The presence of an active uncontrolled infection, including a significant bacterial, fungal, viral or parasitic infection that requires treatment Presence of recurrent primary malignancy, or those treated for recurrence after Hematopoietic Cell Transplantation (HCT), or those who may require rapid removal of immunosuppression as pre-emergency treatment of primary recurrence Have unresolved venous occlusion disease Patients who have any underlying or current medical or psychiatric problems that the researcher thinks may be a disorder (uncontrolled infection, cardiovascular failure, and pulmonary pressure) Patients who have any allergy to blood products

Age
From **18 years** old to **65 years** old

Gender
Both

Phase
1

Groups that have been masked
No information

Sample size
Target sample size: **12**

Randomization (investigator's opinion)
Not randomized

Randomization description

Blinding (investigator's opinion)
Not blinded

Blinding description

Placebo
Not used

Assignment
Single

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics Committee of Shahid Beheshti University of Medical Sciences

Street address
Tehran Province, Tajrish، Velenjak، 7th Floor, Bldg No.2 SBUMS, Arabi Ave

City
Tehran

Province
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Postal code
1985717443

Approval date
2024-05-12, 1403/02/23

Ethics committee reference number
IR.SBMU.REC.1403.011

Health conditions studied

1

Description of health condition studied
Acute steroid-resistant graft-versus-host disease

ICD-10 code
D89.810

ICD-10 code description
Acute graft-versus-host disease

Primary outcomes

1

Description
Recurrence of acute Graft Versus Host Disease (aGVHD) and infection

Timepoint
7, 21 and 28 days after injection

Method of measurement
History, Physical exam, and lab test

2

Description
Overall Remission Rate (ORR)

Timepoint
7, 21 and 28 days after injection

Method of measurement

Assessed using the Glusburg (based on GvHD grade)

Secondary outcomes

1

Description
Progression-free survival (PFS)
Timepoint
48 weeks after exosome infusion
Method of measurement
Assessed using the Graft-versus-Host Disease Working Committee

2

Description
Duration of Response (DOR)
Timepoint
48 weeks after exosome infusion
Method of measurement
Assessed using the Graft-versus-Host Disease Working Committee

Intervention groups

1

Description
Intervention group: Patients diagnosed with grade II to IV acute Graft Versus Host Disease (aGVHD), whose response to treatment with corticosteroids equal or more than 2 milligram per kilogram (mg/kg) is poor and symptoms progress in three days or stable disease for five days, after informed written consent will be included in the study. The diagnosis of Steroid resistant acute graft versus host disease (SR-aGVHD) is based on the diagnosis, grading and staging of aGVHD according to clinical observations and criteria suggested by the International Blood and Bone Marrow Transplant Research Center. Exosome derived from placenta mesenchymal stem cells from donors after obtaining a written consent from the donor, several tests are performed for the absence of contamination. Then the mesenchymal cells are separated under sterile conditions (Good Manufacturing Practices (GMP) grade) and after the characteristic finding in sterile vials will be transferred to the hospital and will be used as an intravenous injection for patients. In each exosome injection, 1 unit of human placenta -derived mesenchymal stem cell exosome (HP-MSC-EXO) is approximately equivalent to the number of exosome particles, which is prepared from 101 x 108 cells, which is administered in the same amount of HP-MSC-EXO in the recipient group weighting 50 to 80 kilogram. The dose of exosome based on studies is 50 microgram per milliliter (µg/mL) and is equivalent to 250-300 milligram of exosome in each vial. Agonists of H1 and H2 receptors are prescribed to prevent allergic reactions before injection and patients are constantly monitored for 2 hours. Exosome injection is done in the form of three doses on the first day after an interval of 8 hours (TDS) and maintenance injection is done daily for 5 days, which dose will be done based on a pilot study conducted in Taleghani Hospital. In this group, the prescription of other treatment protocols, especially Infliximab, is not allowed under any circumstances, and if prescribed, the patient will be excluded from the study. Until the complete failure of the treatment, the prescription of other treatment protocols, especially Infliximab, is prohibited.***The therapeutic intervention method and scientific history and the theoretical basis of the method and its research history as well as the possibility of side effects are accurately and transparently informed to the patient or his companions (often the companions of the patient due to the bad condition of the patients) and the relevant therapeutic intervention it is done with their consent. The information of the patients is collected every day by the researcher who collects the information by filling out a special form. The method of collecting information is based on talking to the patient in his clinic and examining the file to check the symptom registration forms and the results of clinical tests.***Patients assessment in terms of recurrence of aGVHD and infection, complications of cell therapy (safety), recurrence of the disease at intervals of 7+, 21+ and 28+ days after the first exosome injection. Patients are evaluated based on Glusburg criteria (based on GvHD grade) at intervals of +14, +21 and +28 days after the first injection. All patients who receive exosome should wash the route of exosome injection with distilled water immediately before and after injection. Vital signs of patients are constantly checked; Especially, the symptoms one hour after drug injection and as an investigation of the possible effects of the drug are recorded in the results. Any unwanted complication or unusual event is recorded so that it can be recorded in the results if a possible complication occurs. If the condition of the recipient of exosome worsens, the patient will be excluded from the study and the patient will be a candidate for drug or cell therapy.
Category
Treatment - Other

Recruitment centers

1

Recruitment center
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Sponsors / Funding sources

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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Omid cell and tissue tech
Proportion provided by this source
80
Public or private sector
Private
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Persons

2

Sponsor
Name of organization / entity
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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Shahid Beheshti University of Medical Sciences
Proportion provided by this source
20
Public or private sector
Public
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Persons

Person responsible for general inquiries

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Undecided - It is not yet known if there will be a plan to make this available

Study Protocol
Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan
Undecided - It is not yet known if there will be a plan to make this available

Informed Consent Form
Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report
Undecided - It is not yet known if there will be a plan to make this available

Analytic Code
Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available