

Clinical Trial Protocol

Iranian Registry of Clinical Trials

23 Feb 2026

Evaluation of the Safety and Efficiency of human Umbilical Cord Derived Mesenchymal Stem Cell Exosomes in patients with ARDS of COVID-19; An interventional randomized double-blind controlled clinical trial: phase I and II

Protocol summary

Study aim

The use of mesenchymal stem cells-derived exosomes that were cultured in an inflammatory niche, can have beneficial effects in preventing or reducing cytokine storms due to the high modulating potential of the immune system, and reduce the complications and mortality of this disease.

Design

A controlled trial with parallel groups, double-blind, randomized, phases 1 and 2 on 72 patients. The random sequence table was used to randomize the blocks.

Settings and conduct

Stem cells will be cultured in DMEM/F12 with 10% serum. The inflammatory niche will be provided with interleukin 1-beta. Ultracentrifugation purifies the extracellular vesicles of the cell culture supernatant. Centrifugation at 110,000g for 3hours allows the exosomes to precipitate. Exosomes are resolved in PBS and after the QC tests will be prescribed at 100 million/kg. The patient, treating physician, and the physician who follow-up are blinded.

Participants/Inclusion and exclusion criteria

Inclusion Criteria: 1- Definitive infection with COVID-19 confirmed by PCR 2- Acute respiratory distress Syndrome of moderate to severe type (PaO₂/ FiO₂ <200mmHg) 3- Age between 18 to 65 years from both Sexes 4- No Participation in another clinical trial during this study 5- Written informed consent Exclusion Criteria: 1- Malignant diseases 2- Pregnancy 3- Symptoms or history of liver or kidney failure 4- History of lung surgery or Lung transplantation 5- Having an autoimmune disease or Metabolic disorders (such as diabetes) 6- Severe trauma occurred within 14 days before screening 7- Who are undergoing hemodialysis or peritoneal dialysis

Intervention groups

1- Intravenous injection of 2ml normal saline contains umbilical cord mesenchymal stem cell-derived Exosomes

2- Intravenous injection of 2ml normal saline

Main outcome variables

Adverse reaction (AE) and severe adverse reaction (SAE);
Time to clinical improvement (TTIC)

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20201202049568N3**
Registration date: **2021-03-05, 1399/12/15**
Registration timing: **registered_while_recruiting**

Last update: **2021-03-05, 1399/12/15**

Update count: **0**

Registration date

2021-03-05, 1399/12/15

Registrant information

Name

Rashin Mohseni

Name of organization / entity

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2021-03-05, 1399/12/15

Expected recruitment end date

2021-05-05, 1400/02/15

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Evaluation of the Safety and Efficiency of human Umbilical Cord Derived Mesenchymal Stem Cell Exosomes in patients with ARDS of COVID-19; An interventional randomized double-blind controlled clinical trial: phase I and II

Public title

Exosome therapy in ARDS patients

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Acute respiratory distress Syndrome of moderate to severe type (PaO₂/ FiO₂ <200mmHg) Age range between 18 to 65 years Men and Women No participation in another clinical trial during this study Patients who have given themselves and their families a full explanation of the study process and have obtained informed written consent Chest X-ray showed bilateral infiltration with pulmonary edema Definitive infection with COVID-19 confirmed by PCR

Exclusion criteria:

Cancer or malignant diseases Pregnant women or planning to become pregnant Inflammatory diseases Symptoms or history of liver or kidney failure History of lung surgery or Lung transplantation Having an autoimmune disease Metabolic disorders (such as diabetes) Infectious viral infection Proven blood clotting disorders Participate in other clinical trials simultaneously Severe trauma occurred within 14 days before screening They are undergoing hemodialysis or peritoneal dialysis Bone marrow transplantation Have a history of epilepsy, need continuous anticonvulsant therapy

Age

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

Gender

Both

Phase

1-2

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

Sample size

Target sample size: **72**

Randomization (investigator's opinion)

Randomized

Randomization description

In this study, the Stratified Block Randomization method is used to randomize patients in the intervention and

control groups. Because patients with different intensities are in the study, classification is based on the type of need or lack of need for respiratory support. Patients who need respiratory support in the form of mechanical ventilation are classified in group A and patients who need nasal cannula or do not need respiratory support are classified in group B. The blocks used are of sizes 2, 4, and 8, and based on the probable number of people participating in the study with any severity of the disease, blocks with the appropriate volume are used to generate random codes. In order to place patients in control and intervention groups, a random sequence table is created with the help of SAS 9.1 software. Each patient is assigned a completely random sequence number, and random numbers are placed in envelopes (exactly the same, completely closed, with no transparency to view the contents of the envelope). Patients choose one of the envelopes as they wish. Envelopes are kept by a researcher, who does not participate in the study and is not aware of the type of study until the data is collected. Only in case of severe complications, the researcher will be notified through the main project partner to open the relevant envelope.

Blinding (investigator's opinion)

Double blinded

Blinding description

In this study, the participant in the intervention, his / her clinical caregiver, trial researcher, and outcome assessor did not know that they were prescribing the intervention drug or placebo.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Tehran University of Medical Sciences

Street address

Children's Medical Center Hospital, Dr. Gharib Ave, Keshavarz Blvd

City

Tehran

Province

Tehran

Postal code

1419733151

Approval date

2020-11-21, 1399/09/01

Ethics committee reference number

IR.TUMS.MEDICINE.REC.1399.782

Health conditions studied

1

Description of health condition studied

Acute Respiratory Distress Syndrome due to COVID-19

ICD-10 code

U07.1

ICD-10 code description

Acute respiratory distress syndrome

Primary outcomes

1

Description

Adverse reaction (AE) and severe adverse reaction (SAE)

Timepoint

At the beginning of the intervention and on days 2, 3, 4, 7 and 14 after the intervention

Method of measurement

Physical examination of pulmonary function test

Secondary outcomes

1

Description

Murray lung injury score

Timepoint

Baseline and Days 1, 2, 3, 7, 14, 28, and 60 after intervention

Method of measurement

Clinical checklist. The minimum value is 0 and the maximum is 16. Higher scores mean a worse outcome.

2

Description

PaO₂/FiO₂

Timepoint

Baseline and Day 3, Day7, Day14, Day28, Day60

Method of measurement

Oxygen index: the ratio of alveolar oxygen partial pressure to fraction of inspired oxygen

3

Description

The number of days the survivor was out of ICU

Timepoint

60 Days

Method of measurement

The number of days the survivor was out of ICU

4

Description

Blood biochemistry (CRP)

Timepoint

Baseline, day 5, 10, 20

Method of measurement

C-reactive protein (CRP, mg/mL) concentration in the plasma will be measured.

Intervention groups

1

Description

Intervention group: Phase one: 12 patients with COVID-19 in two groups of 6 with ARDS (each group includes intervention groups of 3). Phase Two: 60 patients with COVID-19-ARDS in two groups of 30 controls and intervention. Classified A and B in both control and intervention groups - Exosome receiving group (intervention groups) • Injection material: Umbilical Cord Stem Cell-derived exosomes • Injection rate: 100 million exosomes per kilogram of body weight • Injection carrier: Saline • Injection site: Intravenous

Category

Treatment - Other

2

Description

Control group: Conventional treatments used in ARDS

Category

Treatment - Other

Recruitment centers

1

Recruitment center

Name of recruitment center

Imam Khomeini Complex hospita;

Full name of responsible person

Mehrnaz Asadi Gharabaghi

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Imam Khomeini hospital, Bagherkhan St., Chamran Highway, Tehran

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Tarmim Ava Baran Knowledge Based Company

Full name of responsible person

Abbas Mohammadi Matin

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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
Tarmim Ava Baran Knowledge Based Company
Proportion provided by this source
100
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
Other

Person responsible for general inquiries

Contact
Name of organization / entity
Tehran University of Medical Sciences
Full name of responsible person
Rashin Mohseni
Position
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Latest degree
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Other areas of specialty/work
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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Yes - There is a plan to make this available

Study Protocol

No - There is not a plan to make this available

Statistical Analysis Plan

No - There is not a plan to make this available

Informed Consent Form

Yes - There is a plan to make this available

Clinical Study Report

Yes - There is a plan to make this available

Analytic Code

No - There is not a plan to make this available

Data Dictionary

No - There is not a plan to make this available

Title and more details about the data/document

All data is potentially shareable after the patient turned Unidentifiable.

When the data will become available and for how long

Access period starts 6 months after the results are published

To whom data/document is available

All people

Under which criteria data/document could be used

Physicians and people working in the regenerative medicine industry

From where data/document is obtainable

The person is responsible for the scientific content of the clinical trial. Dr. Alireza Shoaee Hassani
cell.therapy@yahoo.com

What processes are involved for a request to access data/document

The scientific supervisor of the trial transmits the request to the sponsor and with his permission provides the documents to the applicant.

Comments