Clinical Trial Protocol
Iranian Registry of Clinical Trials

31 May 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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rashin_mohseni@yahoo.com

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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Floor 8, No 41, Italia St., Vesal Ave

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1417755362
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cell.therapy@yahoo.com

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
PhD in Applied Cell Science
Latest degree
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Other areas of specialty/work
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Person responsible for scientific inquiries

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Person responsible for updating data

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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 Shoae 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