Clinical Trial Protocol
Iranian Registry of Clinical Trials

31 May 2026

Randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of human umbilical cord MSC–derived exosomes (hUCMSC-Exos) in COVID-19–associated ARDS (Pilot study)

Protocol summary

Study aim

The objective of this study was to evaluate the safety and efficacy of human umbilical cord mesenchymal stem cell–derived exosomes (hUCMSC-Exos) in patients with COVID-19–induced acute respiratory distress syndrome (ARDS), with a particular focus on reducing inflammation, modulating the immune response, and improving clinical outcomes.

Design

This study is a randomized, double-blind, placebo-controlled pilot clinical trial. Patients are assigned to either the intervention group (hUCMSC-Exos) or the control group (placebo), with all participants receiving standard therapy in addition to the assigned intervention or placebo."

Settings and conduct

This study is a randomized, double-blind, placebo-controlled clinical trial conducted at Razi Hospital, Ahvaz, Iran. The study process includes screening, obtaining informed consent, random allocation to either the intervention or control group, administration of a single intravenous dose of hUCMSC-Exos or placebo, and follow-up for up to 7 days to assess clinical and laboratory outcomes

Participants/Inclusion and exclusion criteria

Participants: 18–65 years, both sexes, COVID-19 positive, moderate to severe ARDS, requiring oxygen therapy, bilateral pulmonary infiltrates, written consent.
Exclusions: malignancy, pregnancy, liver/kidney failure, lung surgery/transplant, autoimmune/metabolic disease, coagulation disorder, trauma, viral infection, concurrent trial, dialysis, bone marrow transplant, epilepsy, clotting disorder.

Intervention groups

Group A will receive a single intravenous dose of hUCMSC-derived exosomes (5×10^{10} particles suspended in 2–5 mL PBS) in addition to standard therapy. Group B (control) will receive a placebo consisting of sterile PBS with an identical volume and route of administration, along with standard therapy.

Main outcome variables

The primary outcome is infusion safety and patients' immune-inflammatory response

General information

Reason for update

During the implementation of this trial, which coincided with the peak of the COVID-19 pandemic, numerous clinical studies with overlapping inclusion criteria were simultaneously underway in the country. This overlap created considerable competition for patient recruitment and substantially reduced the pool of eligible participants for the present study. Furthermore, the investigational therapy—human mesenchymal stem cell–derived exosomes—was being introduced for the first time in Iran. Owing to the novelty of this intervention and the lack of familiarity among patients and their families, many preferred to rely on more conventional treatment options, thereby limiting enrollment. In addition, this study was intentionally designed as a pilot trial, with the primary objectives of evaluating safety, assessing feasibility, and providing preliminary insights into therapeutic efficacy as a foundation for larger-scale investigations. Another major challenge pertained to the process of obtaining informed consent: many patients with ARDS were critically ill or unconscious, while quarantine restrictions made timely access to family members difficult. Collectively, these factors led to a reduced final sample size and necessitated the present update of the IRCT record.

Acronym

IRCT registration information

IRCT registration number: **IRCT20190101042197N2**
Registration date: **2021-04-19, 1400/01/30**
Registration timing: **prospective**

Last update: **2025-08-30, 1404/06/08**
Update count: **1**

Registration date
2021-04-19, 1400/01/30

Registrant information
Name
Alireza Shoae-Hassani
Name of organization / entity
Country
Iran (Islamic Republic of)
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Recruitment status
Recruitment complete
Funding source

Expected recruitment start date
2021-05-20, 1400/02/30
Expected recruitment end date
2021-09-22, 1400/06/31
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of human umbilical cord MSC–derived exosomes (hUCMSC-Exos) in COVID-19–associated ARDS (Pilot study)

Public title
Umbilical cord exosomes for reducing inflammation in COVID-19 ARDS
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
18 to 65 years Gender: Both PCR-confirmed COVID-19 moderate-to-severe ARDS (PaO2/FiO2 < 200) SpO2 < 93% on oxygen bilateral infiltrates on imaging written informed consent
Exclusion criteria:
Malignancy pregnancy hepatic/renal failure lung or bone marrow transplant autoimmune/metabolic disease dialysis contagious infection active epilepsy coagulopathy
Age
From **18 years** old to **65 years** old
Gender
Both

Phase
1
Groups that have been masked

- Participant
- Investigator
- Outcome assessor

Sample size
Target sample size: **30**
Randomization (investigator's opinion)
Randomized
Randomization description
Computer-generated sequence (SAS 9.1), stratified block, opaque sealed envelopes, allocation by independent blinded researcher.
Blinding (investigator's opinion)
Double blinded
Blinding description
Double-blind (patients, investigators, outcome assessors).
Placebo
Used
Assignment
Parallel
Other design features
Single IV dose of hUCMSC-derived exosomes (5×10^10 particles in 2–5 mL PBS) + standard of care

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Research Ethics Committees of Ahvaz Jundishapur University of Medical Sciences
Street address
Deputy of Research and Technology Development, Jundishapur University of Medical Sciences, Ahvaz, Ground Floor, Room 4
City
Ahvaz
Province
Khouzestan
Postal code
1579461357
Approval date
2021-03-17, 1399/12/27
Ethics committee reference number
IR.AJUMS.REC.1399.954

Health conditions studied

1

Description of health condition studied
Acute Respiratory Distress Syndrome due to COVID-19
ICD-10 code
J80
ICD-10 code description
Acute respiratory distress syndrome

Primary outcomes

1

Description
Tumor necrosis factor alpha (TNF-α)
Timepoint
Baseline to day 7
Method of measurement
It is measured in serum blood samples using an ELISA kit.

2

Description
CRP
Timepoint
Change from baseline to day 7
Method of measurement
Measurement is performed in serum using an immunoassay kit

3

Description
Serious Adverse Event (SAEs)
Timepoint
Serious adverse events up to day 7
Method of measurement
Recorded from medical records and direct observation

4

Description
IL-6
Timepoint
Change from baseline to day 7
Method of measurement
Measurement is performed in serum using an ELISA kit.

5

Description
CD3+, CD4+, CD8+ lymphocytes
Timepoint
Change from baseline to day 7
Method of measurement
Measurement is performed using a flow cytometry device.

6

Description
D-dimer
Timepoint
Changes from baseline to day 7
Method of measurement
Measurement is performed using the ELISA method

7

Description
PRIEST score
Timepoint
Change up to day 7
Method of measurement
Assessment is performed by the treating physician according to standard guidelines.

8

Description
Chest imaging
Timepoint
Changes on day 3
Method of measurement
Assessment is performed using chest radiography and radiological interpretation.

9

Description
Length of hospital stay
Timepoint
Until discharge.
Method of measurement
Recorded from the clinical file

Secondary outcomes

empty

Intervention groups

1

Description
A total of 30 patients (15 in the intervention group and 15 in the control group) are randomly assigned in a 1:1 ratio. The intervention group receives a single intravenous dose of human umbilical cord mesenchymal stem cell-derived exosomes (hUCMSC-Exos) at 5×10^{10} particles in 2–5 mL PBS along with standard care. The control group receives a placebo (PBS of equal volume) along with standard care. Randomization is block-stratified, and the study is double-blind, so patients, investigators, and outcome assessors are unaware of group allocation.
Category
Treatment - Other

2

Description
Control group: Conventional treatments used in Acute Respiratory Distress Syndrome
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Razi hospital

Full name of responsible person
Reza Khedri
Street address
Amanieh, Palestine Street, opposite the Governorate.
City
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Province
Khouzestan
Postal code
6196514941
Phone
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Razi-hos@ajums.ac.ir

2

Recruitment center
Name of recruitment center
Golestan Hospital
Full name of responsible person
Mofid Husseinzadeh
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Golestan Neighborhood
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Email
mofidhusseinzade@gmail.com

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Danesh Bonyan Company: Tarmim Avaye Baran
Full name of responsible person
Dr. Abbas Mohammadi Matin
Street address
Mirdamad, Paytakht Complex, Block B, 8th Floor
City
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Province
Tehran
Postal code
1417755362
Phone
+98 21 8605 4062
Email
Info@tarmimava.com
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Danesh Bonyan Company: Tarmim Avaye Baran
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
Ahvaz University of Medical Sciences
Full name of responsible person
Mehrdad Dargahi
Position
Assistant professor
Latest degree
Subspecialist
Other areas of specialty/work
Pulmonologist
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Person responsible for scientific inquiries

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Other areas of specialty/work
Cell Therapy and Regenerative Medicine
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Person responsible for updating data

Contact

Name of organization / entity

Ahvaz University of Medical Sciences

Full name of responsible person

Mandana Pouladzadeh

Position

Assistant Professor

Latest degree

Specialist

Other areas of specialty/work

Emergency Medicine

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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

No - There is not 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

Some of the data can potentially be shared after de-identification of individuals.

When the data will become available and for how long

The access period will begin 6 months after the publication of the results.

To whom data/document is available

All people

Under which criteria data/document could be used

Hospitals for clinical purposes and researchers for the accelerated advancement of projects.

From where data/document is obtainable

Scientific responsibility for the clinical trial: Stem Cell and Regenerative Medicine Research Center, Iran University of Medical Sciences, Shahid Motahari Hospital.

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

A written request specifying the reasons for the need for the data.

Comments