# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

02 Oct 2026

## Investigating the effect of adding subcutaneous ketamine to routine treatment of treatment-resistant depressed patients

### Protocol summary

**Study aim**
1.Determination and Comparison of mean depression scores between intervention and control groups before the intervention, at weeks 2, 4, 6, and one month after the last session. 2.Determination and Comparison of the mean number of adverse events between intervention and control groups at the same time points.

**Design**
A clinical trial with control group, with the parallel groups, Double-blind, randomized

**Settings and conduct**
in a double-blind clinical trial at Khorshid Hospital in Isfahan enrolls 52 patients with treatment-resistant major depressive disorder, who are randomly assigned to two parallel groups. Depression severity and adverse effects are evaluated at baseline, during weeks 2, 4, and 6 of treatment, and one month after the final intervention.

**Participants/Inclusion and exclusion criteria**
Inclusion criteria: 1.Age between 60-18 years 2.Individual who have DSM-V indicators for major depression without psychotic characteristics and mania or hypomania 3.Individual who do not have an adequate response to monotherapy with antidepressants for at least two times (at least 4-6 weeks) 4.Satisfaction with participating in the study Exclusion criteria: 1.Pregnant or breastfeeding women 2.History of substance dependence or abuse in the last 3 months 3.Serious and unstable physical patients 4.Untreated hypothyroidism or hyperthyroidism 5.Current or past history of psychotic symptoms 6.History of mania or hypomania, catatonia, or depression secondary to a medical condition 7.History of hypertension 8.History of seizure disorder 9. renal failure

**Intervention groups**
In the intervention group, ketamine(0.5 mg/kg) is administered subcutaneously, and in the control group, normal saline is administered subcutaneously, both twice weekly for six weeks

**Main outcome variables**
severity of depression: side effects

### General information

**Reason for update**

**Acronym**

**IRCT registration information**
IRCT registration number: **IRCT20090801002266N22**
Registration date: **2026-02-09, 1404/11/20**
Registration timing: **prospective**

Last update: **2026-02-09, 1404/11/20**
Update count: **0**

**Registration date**
2026-02-09, 1404/11/20

**Registrant information**

**Name**
Gholamreza Kheirabadi

**Name of organization / entity**

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Iran (Islamic Republic of)

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**Recruitment status**
**recruiting**

**Funding source**

**Expected recruitment start date**
2026-04-04, 1405/01/15

**Expected recruitment end date**
2027-04-04, 1406/01/15

**Actual recruitment start date**
empty

**Actual recruitment end date**
empty

**Trial completion date**

empty

**Scientific title**
Investigating the effect of adding subcutaneous ketamine to routine treatment of treatment-resistant depressed patients

**Public title**
ketamine injection on improving treatment-resistant depression

**Purpose**
Treatment

**Inclusion/Exclusion criteria**

**Inclusion criteria:**
Age between 60-18 years Individuals who have DSM-V indicators for major depression without psychotic characteristics and mania or hypomania individuals who do not have an adequate response to monotherapy with antidepressants for at least two times (at least 4-6 weeks) Satisfaction with participating in the study

**Exclusion criteria:**
Pregnant or breastfeeding women History of substance dependence or abuse in the last 3 months Serious and unstable physical patients including liver, kidney, gastrointestinal, respiratory, cardiovascular diseases (such as ischemic heart disease), endocrine, neurological, hematological Untreated hypothyroidism or hyperthyroidism Current or past history of psychotic symptoms History of mania or hypomania, catatonia, or depression secondary to a medical condition History of hypertension History of seizure disorder Diagnosis of renal failure

**Age**
From **18 years** old to **60 years** old

**Gender**
Both

**Phase**
3

**Groups that have been masked**

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

**Sample size**
Target sample size: **52**

**Randomization (investigator's opinion)**
Randomized

**Randomization description**
Eligible participants will be randomized using block randomization with a block size of two. Within each block, participants are ordered by national ID number. A random number table is used to determine the allocation sequence. Two possible sequences exist (A-B,B-A) , and neither participants nor investigators know which label(A orB) corresponds to ketamin or placebo . A third party who is aware of the treatment codes prepares the study medications in sealed opaque envelopes and delivers them to the research team, maintaining double blinding. This process continues until all participants have received their assigned intervention.

**Blinding (investigator's opinion)**
Double blinded

**Blinding description**
Both participants and investigators involved in outcome assessment are unaware of the treatment assignments. Study medications, labeled as A and B, are prepared by a third party who is not involved in patient evaluation. The third party is aware of the correspondence between the labels and the actual interventions (drug or placebo). The medications are placed in sealed opaque envelopes and delivered to the research team for administration. Blinding is maintained until all study outcomes have been collected.

**Placebo**
Used

**Assignment**
Parallel

**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**

**Name of ethics committee**
Research Ethics Committee of School of Medicine ,Isfahan University of Medical Sciences

**Street address**
Isfahan University of Medical Sciences, Hezar Jerib street

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**Province**
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8174673461

**Approval date**
2026-01-27, 1404/11/07

**Ethics committee reference number**
IR.MUI.MED.REC.1404.436

## Health conditions studied

### 1

**Description of health condition studied**
Treatment-Resistant Major Depressive Disorder

**ICD-10 code**
F33.9

**ICD-10 code description**
Major depressive disorder, recurrent, unspecified

## Primary outcomes

### 1

**Description**
Depression score (assessed using the HDRS)

**Timepoint**
Before the intervention, at week 2, week 4, and week 6 during the intervention, and one month after the last intervention session
**Method of measurement**
Hamilton Depressive Rating Scale (HDRS)

## Secondary outcomes

### 1

**Description**
Intervension side effects
**Timepoint**
Before the intervention, at week 2, week 4, and week 6 during the intervention, and one month after the last intervention session
**Method of measurement**
checklist evaluation

## Intervention groups

### 1

**Description**
Intervention group: In this group, ketamine at a dose of 0.5 mg/kg is administered subcutaneously twice weekly for six weeks, for a total of 12 injections.
**Category**
Treatment - Drugs

### 2

**Description**
Control group: n this group, Placebo (normal saline) is administered subcutaneously twice weekly for six weeks, for a total of 12 injections.
**Category**
Placebo

## Recruitment centers

### 1

**Recruitment center**
**Name of recruitment center**
Khorshid Hospital
**Full name of responsible person**
Gholamreza Kheirabadi
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## Sponsors / Funding sources

### 1

**Sponsor**
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Esfahan University of Medical Sciences
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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**
Esfahan University of Medical Sciences
**Proportion provided by this source**
100
**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**
Academic

## Person responsible for general inquiries

**Contact**
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Esfahan University of Medical Sciences
**Full name of responsible person**
Gholamreza Kheirabadi
**Position**
Professor
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## Person responsible for updating data

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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**
No - There is not a plan to make this available
**Justification/reason for indecision/not sharing IPD**
There is no further information
**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**
No - There is not 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