Clinical Trial Protocol
Iranian Registry of Clinical Trials

26 May 2026

Comparing Efficacy of Extended-release Injectable Naltrexone (XR-NTX) with Oral Naltrexone on Opioid Abstinence among People with Opiate Use Disorder: A Triple-blind Randomized Controlled Trial

Protocol summary

Study aim

Determining the efficacy of treatment with extended-release injectable naltrexone compared to oral naltrexone and placebo in the treatment of opiate use disorder

Design

A phase 3, parallel group, triple blind randomized controlled trial in which 150 participants are randomly assigned to one of three study arms using www.sealedenvelope.com website.

Settings and conduct

Randomized controlled clinical trial in Iranian National Center for Addiction Studies (INCAS)'s clinic.

Participants/Inclusion and exclusion criteria

Inclusion criteria: • Age 18 to 65 years • Diagnosis of moderate to severe opiate use disorder, tendency to antagonist maintenance treatment, and completion of medically-assisted opioid withdrawal • Good physical health and hematology testing, liver and kidney function in the normal range • To use contraception in women • Living in Tehran • To have a family member or companion for regular visits and medication monitoring • ECG without severe abnormalities • Ability to understand and give informed consent Exclusion criteria: • Positive antagonist challenge test or positive urine test for opioids • Receiving opioids medications • Alcohol, stimulants or sedatives and hypnotics use disorder • Pregnancy or lactation • Uncontrolled major psychiatric disorder • Severe uncontrolled physical condition • Probability of surgery during the study period • Obesity or low weight for muscle injection • Sensitivity to study medications • Being on probation or under judicial supervision

Intervention groups

1- Extended-release injectable naltrexone + oral placebo 2- Injectable placebo + oral naltrexone 3- Injectable placebo + oral placebo

Main outcome variables

Average number of abstinence weeks (weekly till 24 weeks); Percentage of patients who have completed treatment.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20170702034844N6**
Registration date: **2020-07-31, 1399/05/10**
Registration timing: **registered_while_recruiting**

Last update: **2020-07-31, 1399/05/10**
Update count: **0**

Registration date

2020-07-31, 1399/05/10

Registrant information

Name

Alireza Noroozi

Name of organization / entity

Iranian National Center for Addiction Studies (INCAS)

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-07-22, 1399/05/01

Expected recruitment end date

2021-12-22, 1400/10/01

Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Comparing Efficacy of Extended-release Injectable Naltrexone (XR-NTX) with Oral Naltrexone on Opioid Abstinence among People with Opiate Use Disorder: A Triple-blind Randomized Controlled Trial

Public title
Comparing Efficacy of Extended-release Injectable Naltrexone (XR-NTX) with Oral Naltrexone
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Diagnosis of moderate to severe opiate use disorder including only opium, Shireh (opium concentrate), heroin, and/or heroin crack based on DSM 5 Voluntarily seeking treatment and willingness to receive antagonist maintenance treatment Successful completion of medically-assisted opioid withdrawal (including a personal report of at least 7 days of abstinence from opioids, negative urinalysis test for morphine, methadone, buprenorphine and tramadol, and negative antagonist challenge test) Good physical health based on medical records, physical examination and measurement of vital signs Hematology tests, liver and kidney function tests in the normal range In women of childbearing age agree to receive a safe method of contraception Living in Tehran Having a family member or companion who can monitor regular visits and daily use of the study medication No severe abnormalities in the ECG Ability to understand and give written informed consent to enter the study
Exclusion criteria:
Positive antagonist challenge test Positive urinalysis test for opioids (morphine) or opioid drugs (methadone, buprenorphine, tramadol) Patients undergoing maintenance treatment with opioid drugs (methadone, buprenorphine, or opium tincture) Request treatment and desire to receive opioids maintenance treatments with medication like methadone and buprenorphine People treated with opioid antagonists or a history of continuous naltrexone injections in the past 6 months Need to receive opioid medications for medical purposes such as chronic pain disorder Concurrent diagnosis of other substance use disorders such as stimulants and sedatives (except nicotine and caffeine) Concurrent alcohol use disorder and people who are currently need medical management for alcohol withdrawal Pregnancy, lactation or women of childbearing age who are planning to become pregnant or do not use a contraceptive method Having uncontrolled, major psychiatric disorders at the time of referral (e.g. mood disorders with impaired function, schizophrenia, etc.) that can interfere with participation in the study Severe and uncontrolled physical conditions based on physical examination by study's physician and laboratory evaluations (e.g. uncontrolled hypertension or diabetes mellitus) Having uncontrolled medical illness that can interfere with study or significantly increase medical risk. (Such as high blood pressure and uncontrolled diabetes) Severe physical illness (including acute renal failure, endocarditis and tuberculosis) Liver failure, acute hepatitis or more than threefold increase in liver enzymes Thrombocytopenia and a history of coagulation disorders Planning for surgery during the study period Inadequate physical condition for safe intramuscular injection of extended-release naltrexone, body mass index above 40 (excessive adipose tissue in the buttocks) or severe weight loss The presence of AIDS-indicator disease Known sensitivity to naltrexone, polylactide-co-glycolide, arboxymethylcellulose, or other components of the effective and soluble extended-release injectable naltrexone Serious suicidality or a history of suicide last year Last year history of drug overdose that led to hospitalization Being on probation or under judicial supervision with the possibility of re-arrest and re-imprisonment Inability to understand the study protocol or respond to evaluations as well as lack of proper communication with therapists
Age
From **18 years** old to **65 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

Sample size
Target sample size: **150**
Randomization (investigator's opinion)
Randomized
Randomization description
Random codes are created by the person responsible for data randomization using the website www.sealedenvelope.com. Patients are randomly allocated to one of three study arms including injectable naltrexone + oral placebo, injectable placebo + oranl naltrexone and injectable placebo + oral placebo based on random sequence blocks with block size of 6. The codes created by the person responsible for the randomization, are attached to the medications of all three study groups, and each patient's code is given to the treatment provider in a sealed envelope, consecutively.
Blinding (investigator's opinion)
Triple blinded
Blinding description
Patients in all three groups receive either oral naltrexone or oral placebo as same size, color and shape gel capsules. Patients in all three groups also receive either injectable naltrexone or injectable placebo. The

injectable medications are prepared by a nurse and covered with an opaque tape, in order to make injectable naltrexone and injectable placebo indistinguishable.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Vice- chancellor in research affairs, Tehran University of Medical Sciences

Street address
Keshavarz Blvd

City
Tehran

Province
Tehran

Postal code
1467664961

Approval date
2020-05-05, 1399/02/16

Ethics committee reference number
IR.TUMS.VCR.REC.1399.343

Health conditions studied

1

Description of health condition studied
Moderate and severe opiates use disorder

ICD-10 code
F11.2

ICD-10 code description
Opioid dependence

Primary outcomes

1

Description
Proportion of weeks of opioids use abstinence measured by self-report and negative urine test for morphine

Timepoint
Weekly till 24 weeks

Method of measurement
Self report and morphine urine test

2

Description
Treatment completion

Timepoint
Termination of the study

Method of measurement
Checklist for weekly visits

Secondary outcomes

1

Description
Retention in treatment

Timepoint
Weekly till week 24

Method of measurement
Weekly visits check list

2

Description
Craving (severity)

Timepoint
Weekly till 24 week

Method of measurement
Visual analogue scale (VAS)

3

Description
Number of days using opioids during last week

Timepoint
Weekly (week 5 to 24)

Method of measurement
Clinical interview (week 5 to 24)

4

Description
Abstinence from opioids use measured by urine test

Timepoint
Weekly (week 5 to 24)

Method of measurement
Urine tests

5

Description
Adherence to treatment

Timepoint
Weekly

Method of measurement
Weekly physician's visit and patient's self-report on medication use adherence

6

Description
Time to dropping out of study due to positive naltrexone challenge test

Timepoint
Weekly till week 24

Method of measurement
Physician's visit

7

Description
Time to dropping out of study for any reason
Timepoint
Weekly till week 24
Method of measurement
Physician's visit

Intervention groups

1

Description
Intervention group: Injectable naltrexone + oral placebo: Participants in this group receive extended release naltrexone (Exopio, Nano daroo pazhouhan, 380 mg, IM) every 4 weeks and oral placebo. After preparation, extended-release naltrexone is covered by an opaque tape and is given to physician or another nurse within study site. Patients in this group is received daily placebo capsule.
Category
Treatment - Drugs

2

Description
Intervention group: Injectable placebo + oral naltrexone: Participants in this group receive injectable placebo (vial 2 of Exopio medication package) covered by an opaque tape every 4 weeks and oral naltresone capsule 50 mg per day
Category
Treatment - Drugs

3

Description
Control group: Injectable placebo + oral placebo: Participants receive injectable placebo (vial 2 of Exopio package) covered with opaque tape every 4 weeks and oral placebo capsule daily.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Iranian National Center for Addiction Studies' Clinic
Full name of responsible person
Behrang Shadloo
Street address
Kargar St
City
Tehran
Province
Tehran
Postal code
1336616357
Phone
+98 21 5542 1144
Email
behrang.shadloo@gmail.com

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Nanodaroo Pazhouhan Pardis Company
Full name of responsible person
Navid Goodarzi
Street address
Attar Street
City
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Tehran
Postal code
1417614411
Phone
+98 21 8864 9082
Email
goodarzi_n@razi.tums.ac.ir
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Nanodaroo Pazhouhan Pardis Company
Proportion provided by this source
85
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
Industry

2

Sponsor
Name of organization / entity
Tehran University of Medical Sciences
Full name of responsible person
Mohammad Ali Sahraian
Street address
Keshavarz Blvd
City
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Tehran
Postal code
1467664961
Phone
+98 21 8163 3685

Email
vcr@tums.ac.ir
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Tehran University of Medical Sciences
Proportion provided by this source
15
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
Name of organization / entity
Iranian National Center for Addiction Studies
Full name of responsible person
Alireza Noroozi
Position
Psychiatrist
Latest degree
Specialist
Other areas of specialty/work
Psychiatrics
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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
Yes - There is 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
Yes - There is 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
Title and more details about the data/document
It is planned to share IPD, study protocol and report of the clinical study.
When the data will become available and for how

long

IPD will be shared after completion of the data gathering phase. Study protocol will be available within 3 months after successful registration of the trial. Report of the clinical study will be finalized at the end of study .

To whom data/document is available

Clinical researchers

Under which criteria data/document could be used

IPD will be available for researchers who are conducting review studies. Study protocol and report will be published as English articles.

From where data/document is obtainable

Email to the individual who is responsible for scientific inquiries of this project

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

It will be responded after processing within the project team.

Comments