Clinical Trial Protocol
Iranian Registry of Clinical Trials

21 Jul 2026

Efficacy of palliative pharmacotherapy with Methylphenidate, Bupropion, Ginseng, and Amantadine to improve fatigue in people with advanced cancer (5-EPIFAT)

Protocol summary

Study aim

- Comparison of the efficacy of different pharmacological agents (Methylphenidate, Bupropion, Ginseng, Amantadine) versus placebo for managing cancer-related fatigue - Comparison of the efficacy of pharmacological agents relative to each other for managing cancer-related fatigue

Design

A 5-arm, randomised, placebo-controlled trial will use a parallel-group design with an equal allocation ratio. Eligible Patients are randomly assigned to one of the study groups using permuted block randomization method.

Settings and conduct

This trial will be conducted in 5 academic sites (3 hospitals and 2 outpatient oncology clinics) in 3 provinces of Iran (Khuzestan located in the southwest, Tehran located in the north-central and Yazd located in the center). In this study, 4 intervention groups will receive different palliative medication treatments for 4 weeks. Patients in the control group also receive placebo for 4 weeks.The primary outcome is the fatigue level, which is measured over time. All research team personnel except the pharmacist and randomization provider are blind to the group assignment.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Age over 18 years with advanced cancer, and report of moderate to severe fatigue in the last week. Exclusion criteria: A known fatigue disorder not related to cancer, untreated severe anemia or anemia requiring blood transfusion, and hypersensitivity to sympathomimetic amines.

Intervention groups

Four intervention groups will receive different palliative medication treatments for 4 weeks. The first group will receive methylphenidate, the second group will receive bupropion, the third group will receive ginseng, and the fourth group will receive amantadine. Patients in the control group also receive placebo for 4 weeks.

Main outcome variables

Fatigue level

General information

Reason for update

Editing some details

Acronym

5-EPIFAT

IRCT registration information

IRCT registration number: **IRCT20150302021307N6**
Registration date: **2023-05-13, 1402/02/23**
Registration timing: **prospective**

Last update: **2023-09-01, 1402/06/10**
Update count: **1**

Registration date

2023-05-13, 1402/02/23

Registrant information

Name

Mojtaba Miladinia

Name of organization / entity

Ahvaz Jundishapur University of Medical Sciences

Country

Iran (Islamic Republic of)

Phone

+98 613333333

Email address

miladinia.m@ajums.ac.ir

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-09-16, 1402/06/25

Expected recruitment end date
2024-03-15, 1402/12/25
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Efficacy of palliative pharmacotherapy with Methylphenidate, Bupropion, Ginseng, and Amantadine to improve fatigue in people with advanced cancer (5-EPIFAT)

Public title
Palliative pharmacotherapy for cancer-related fatigue
Purpose
Supportive
Inclusion/Exclusion criteria
Inclusion criteria:
Age over 18 years with advanced cancer diagnosis undergoing active anticancer treatment Participants with all types of cancer except patients with central nervous system tumor or hormone-sensitive cancers or Pheochromocytoma Report of moderate to severe fatigue in the last week (score ≥ 4 on a scale of 0 to 10) Diagnosis of cancer-related fatigue based on International Classification of Diseases 10th edition (ICD-10) criteria Hemoglobin level above 9 g/dL in 2 weeks before enrollment Ability to swallow and absorb medications Females who are likely to become pregnant should use contraceptive methods during treatment and up to 6 weeks after. Ability to read and write
Exclusion criteria:
A known fatigue disorder not related to cancer Presence of cognitive disorders, mental disorders (severe anxiety, major depression, schizophrenia, bipolar syndrome), neurological or brain disorders (dementia, delirium, Tourette syndrome, motor tics, epilepsy, history of stroke, aneurysm) Diabetes, untreated severe anemia or anemia requiring blood transfusion, severe and uncontrolled pain and insomnia, serious cardiac disorders, uncontrolled arrhythmia or hypertension, history of long QT syndrome, glaucoma, intestinal obstruction, uncontrolled hypothyroidism, respiratory disorders limiting participation, autoimmune diseases, bleeding disorders Abnormal liver or kidney function History of a major surgery in the month before enrollment Taking erythropoietin, psychostimulants, antidepressants, nutritional supplements, or other medications to control fatigue currently or in the 4 weeks before participating in the study Simultaneous use of drugs (warfarin, anticonvulsants, tricyclic antidepressants, antipsychotics, monoamine oxidase inhibitors, clonidine, theophylline, caffeine and pseudoephedrine) Major dose change (more than 25%) of opioids within 48 hours before enrollment. Hypersensitivity to sympathomimetic amines Planned surgery within 2 months of screening History of sensitivity or intolerance to the drugs under study Pregnant or lactating women History of drug or alcohol abuse in the past year Involved in another clinical trial

Age
From **18 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Investigator
- Data analyser
- Data and Safety Monitoring Board

Sample size
Target sample size: **255**
Randomization (investigator's opinion)
Randomized
Randomization description
255 patients are randomly assigned to 1 of the 5 study groups using a permuted block randomization method and equal allocation ratio (51 patients in each group). The size of the blocks is randomly selected using the Blockrand package in R software (block size = 7, 14, 21, and 28), and therefore the allocation ratio is equal (1:1:1:1:1). The study statistician generate the random allocation sequence using free statistical software R. Then the statistician sends the randomization algorithm to the study pharmacist and the allocator. Each participant who has given written consent to participate in the study is uniquely identified with a two-part code. Blinded research assistants will send a randomization request to the randomization provider, who will immediately receive the order via email, and assign participants to one of 5 study groups (groups identified by a code). Participants and all study personnel (except pharmacist and allocator) are blinded to group assignment.
Blinding (investigator's opinion)
Triple blinded
Blinding description
The statistician sends the randomization list to the pharmacist and randomization provider. The pharmacist will not have a role in data collection and analysis. Also, the randomization provider will not play a role in the rest of the trial. Each participant who has given written consent to participate in the study is uniquely identified with a two-part code. Blinded research assistants will send a randomization request to the randomization provider, who will immediately receive the order via email, and assign participants to one of 5 study groups (groups identified by a code). Other personnel of the research team will be blind until the end of the data analysis. Also, to blind the participants and other members of the research team, the medications will be placed by the pharmacist in opaque and similar capsules in opaque and similar boxes with different coding. Medication codes and randomization list will be kept with the pharmacist until the trial is closed.
Placebo
Used
Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics committee of Ahvaz Jundishapur University of Medical Sciences

Street address
Golestan Blvd.

City
Ahvaz

Province
Khouzestan

Postal code
61357-15794

Approval date
2023-03-04, 1401/12/13

Ethics committee reference number
IR.AJUMS.REC.1401.587

Health conditions studied

1

Description of health condition studied
Cancer-related fatigue

ICD-10 code
R53

ICD-10 code description
Malaise and fatigue

Primary outcomes

1

Description
Fatigue level over time, which will be measured by the functional assessment of chronic illness therapy-fatigue scale.

Timepoint
Fatigue level will be measured at baseline, weekly during the 4-week intervention period, and sixth and eighth weeks as follow-up. Totally, fatigue level will be measured for 7 times.

Method of measurement
The functional assessment of chronic illness therapy-fatigue scale

Secondary outcomes

1

Description
To evaluate the safety, the secondary outcome is the adverse events, which will be assessed by the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events. (Adverse events will be evaluated in 14 subgroups including oral, respiratory, neurological, sleep, sexual, cardio, visual, mood, cutaneous, gastrointestinal, attention, pain, genitourinary, and miscellaneous).

Timepoint
Adverse events will be assessed at baseline, and weekly during the 4-week intervention period.

Method of measurement
The Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events

Intervention groups

1

Description
First intervention group: They will receive oral methylphenidate for 4 weeks. Methylphenidate is started at a dose of 10 mg per day in the first week. After that, the dose of 10 mg twice a day is continued in the second and third week. After that, in the fourth week, the dose returns to 10 mg per day.

Category
Treatment - Drugs

2

Description
Second intervention group: They will receive oral bupropion for 4 weeks. Bupropion is started at a dose of 150 mg per day in the first week. After that, the dose of 150 mg twice a day is continued in the second and third week. After that, in the fourth week, the dose returns to 150 mg per day.

Category
Treatment - Drugs

3

Description
Third intervention group: They will receive oral amantadine for 4 weeks. Amantadine is started at a dose of 100 mg per day in the first week. After that, the dose of 100 mg twice a day is continued in the second and third week. After that, in the fourth week, the dose returns to 100 mg per day.

Category
Treatment - Drugs

4

Description
Fourth intervention group: They will receive oral ginseng for 4 weeks. Ginseng is started at a dose of 500 mg per day in the first week. After that, the dose of 500 mg twice a day is continued in the second and third week. After that, in the fourth week, the dose returns to 500 mg per day.

Category
Treatment - Drugs

5

Description
Control group: They will receive oral placebo. Placebo will start one capsule daily in the first week. After that, two capsules per day will continue in the second and third week. After that, one capsule will be consumed again in the fourth week.

Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Shahid Baghai 2 Hospital
Full name of responsible person
Hossein Karimpourian
Street address
Shahid Baghai 2 Hospital., Khoramshahr Blvd
City
Ahvaz
Province
Khouzestan
Postal code
61357-15794
Phone
+98 61 3373 8622
Email
miladimojtaba@gmail.com

2

Recruitment center
Name of recruitment center
Shafa Clinic
Full name of responsible person
Mojtaba Miladinia
Street address
Shafa clinic, Farvardin St., Golestan Blvd.
City
Ahvaz
Province
Khouzestan
Postal code
61357-15600
Phone
+98 61 3373 7727
Email
miladimojtaba@gmail.com

3

Recruitment center
Name of recruitment center
Department of Clinical Oncology
Full name of responsible person
Hossein Karimpourian
Street address
Department of clinical oncology, Golostan hospital, Farvardin St., Golestan Blvd.
City
Ahvaz
Province
Khouzestan
Postal code
613357-14242
Phone
+98 61 3373 7725
Email
miladimojtaba@gmail.com

4

Recruitment center
Name of recruitment center
Hazrate Rasool Hospital
Full name of responsible person
Marziyeh Ghalamkari
Street address
Corner of Mansouri St., Niyaish St., Sattar Khan Blvd.
City
Tehran
Province
Khouzestan
Postal code
1445613131
Phone
+98 21 6435 1000
Email
dr.ghalam@yahoo.com

5

Recruitment center
Name of recruitment center
Shahid Sadooghi Hospital
Full name of responsible person
Ali Farahat
Street address
Central Administration, Bahonar Sq.
City
Yazd
Province
Khouzestan
Postal code
8915887857
Phone
+98 35 3725 8410
Email
Alifarahat1359@gmail.com

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Ahvaz University of Medical Sciences
Full name of responsible person
Mehrnoosh Zakerkish
Street address
Golestan Blvd.

City
Ahvaz
Province
Khouzestan
Postal code
6135715794
Phone
+98 61 3311 0000
Email
research@ajums.ac.ir
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Ahvaz 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
Name of organization / entity
Ahvaz University of Medical Sciences
Full name of responsible person
Mojtaba Miladinia
Position
Faculty member
Latest degree
Ph.D.
Other areas of specialty/work
Nursery
Street address
School of Nursing, Ahvaz University of Medical Science, Golestan Blvd.
City
Ahvaz
Province
Khouzestan
Postal code
6135715794
Phone
+98 61 3311 0000
Fax
Email
miladinia.m@ajums.ac.ir

Person responsible for scientific inquiries

Contact
Name of organization / entity
Ahvaz University of Medical Sciences
Full name of responsible person
Hossein Karimpourian
Position
Faculty member
Latest degree
Subspecialist
Other areas of specialty/work
Hematology
Street address
School of Nursing, University of Medical Science, Golestan Blvd.
City
Ahvaz
Province
Khouzestan
Postal code
6135715794
Phone
+98 61 3311 0000
Fax
Email
karimpoorian.h@ajums.ac.ir

Person responsible for updating data

Contact
Name of organization / entity
Ahvaz University of Medical Sciences
Full name of responsible person
Mojtaba Miladinia
Position
Faculty member
Latest degree
Ph.D.
Other areas of specialty/work
Nursery
Street address
School of Nursing, University of Medical Science, Golestan Blvd.
City
Ahvaz
Province
Khouzestan
Postal code
6135715794
Phone
+98 61 3311 0000
Fax
Email
miladinia.m@ajums.ac.ir

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
Yes - There is 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

Yes - There is a plan to make this available

Data Dictionary

Yes - There is a plan to make this available

Title and more details about the data/document

The data file will be subscribed to by the SPSS software format.

When the data will become available and for how long

The access period begins after the publication of the findings in the form of a published article.

To whom data/document is available

Data will be available to researchers working in the academic institutions.

Under which criteria data/document could be used

Data will only be available for use in the review and meta-analysis studies.

From where data/document is obtainable

Mojtaba Miladinia via academic email: miladinia.m@ajums.ac.ir

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

First, send an e-mail to the author and mention the purpose of obtaining the information. In the absence of a problem, you will receive information one to three weeks later.

Comments