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MePFAC - A Drug Trial for the treatment of cancer-related Fatigue

Submission date 17/07/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 10/08/2017	**Overall study status** Completed	
Last Edited 04/07/2024	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-a-drug-called-methylphenidate-for-people-with-tiredness-caused-by-cancer-mepfac

Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
2017-001950-33

Integrated Research Application System (IRAS)
215297

Protocol serial number
CPMS 34827, IRAS 215297

Study information

Scientific Title
Methylphenidate versus placebo for fatigue in advanced cancer (MePFAC)

Study objectives
The study aims to estimate clinical effectiveness of methylphenidate versus placebo in the treatment of cancer-related fatigue in patients receiving specialist palliative care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - City & East Research Ethics Committee, 07/08/2017, ref: 17/LO/0871

Study design
Randomized; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Psychosocial Oncology and Survivorship

Interventions

MePFAC is a prospective, randomised, double-blind, placebo-controlled trial with internal pilot in palliative care patients with advanced cancer.

The MePFAC study aims to recruit 230 patients across ten sites in England between 2018 and 2020. Feasibility of recruitment strategy, randomisation and follow-up are evaluated during a pilot phase at four sites during the first nine months of recruitment.

Randomisation is undertaken using an independent data management company ("Sealed Envelope") who have been commissioned by the Priment Clinical Trials Unit to support randomisation and data management for the MePFAC study. Treatment allocation (1:1) is done using a permuted-block randomisation stratified to four factors; the centre, receipt of palliative cancer treatment, baseline HADS depression score, and whether patients are considered to be "severely" fatigued (initial fatigue score >7/10 on a numerical rating scale).

In both trial arms participants are monitored on a weekly basis either by telephone contact (weeks 1, 2, 4, 5, 7 & 8) or at a face-to-face visit (weeks 0, 3, 6 & 9).

Participants in both arms are prescribed identical-looking tablets of either methylphenidate 5mgs or placebo. At weekly intervals (± 3 days) after study medication has been dispensed, participants are contacted by telephone (weeks 1, 2, 4, 5, 7 and 8) or face-to-face (weeks 3, 6 and 9) and the study medication (or placebo) are titrated by the PI in response to information provided by the research staff.

Study medication is dispensed at the baseline assessment, week 3 (± 3 days) and week 6 (± 3 days). The three days' flexibility on either side of the scheduled assessment days is to allow for contingencies. On visit days, pill counts are performed to assess compliance to IMP.

At the face-to face assessment at the end of week 9 (±3 days) the study will end. At that point participants are assessed by the local clinical service and a decision is made about whether or not methylphenidate should be prescribed depending upon local clinical assessment and patient and physician preference.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Methylphenidate

Primary outcome(s)
To compare fatigue, measured by Functional Assessment of Chronic Illness Therapy (FACIT-F), in patients with advanced cancer receiving individually titrated doses of methylphenidate with patients receiving placebo after six weeks' treatment.

Key secondary outcome(s))
1. Quality of life is measured using the European Organisation for Research and Treatment of Cancer core Quality of Life Palliative Care questionnaire [EORTC QLQ-C15-PAL] and the EuroQol EQ-5D 5 level [EQ-5D-5L]) at 3, 6 and 9 weeks
2. Adverse events are documented on the case report form (as mild, moderate or severe) at 3, 6

and 9 weeks
3. Activities of daily living is measured using the mobility, self-care and usual activity domains of the EQ-5D-5L at 3, 6 and 9 weeks
4. Appetite is measured using the anorexia item on the EORTC QLQ-C15-PAL at 3, 6 and 9 weeks
5. Satisfaction of patients and carers are measured using the Global benefit score (GBS) at 3, 6 and 9 weeks
6. Survival of patients after recruitment is measured by asking patients for permission to flag their records with the NHS Information Centre (NHS IC) at 3, 6 and 9 weeks
7. Need for other medication specifically steroids, antidepressants, anxiolytics and analgaesics) will be measured by asking participants about concomitant medication use at baseline and at week six

Completion date
31/10/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 28/10/2018 (updated 27/07/2023):
1. Aged 18 years or over
2. Participant is willing and able to give informed consent for participation
3. Advanced incurable cancer of all tumour types
4. Moderate or severe fatigue (>3/10 on a numerical rating scale)
5. Able and willing to comply with all study requirements, including ability to participate in study for ten weeks
6. Participant is receiving generalist or specialist palliative care
7. Willing to allow his or her General Practitioner to be notified of participation in the study

Previous inclusion criteria:
1. Aged 18 years or over
2. Participant is willing and able to give informed consent for participation
3. Advanced incurable cancer of all tumour types
4. Moderate or severe fatigue (>3/10 on a numerical rating scale)
5. Prognosis 2-12 months (as estimated by clinician)
6. Able and willing to comply with all study requirements, including ability to participate in study for nine weeks
7. Under the care of a specialist palliative care team
8. Willing to allow his or her General Practitioner to be notified of participation in the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
162

Key exclusion criteria
Current exclusion criteria as of 28/10/2018 (updated 27/07/2023):
1. Pregnancy
2. Females of childbearing potential and males who have sexual partners with child-bearing potential must be willing to use an effective method of contraception (hormonal or barrier method of birth control; true abstinence) from the time consent is signed until six weeks after treatment discontinuation and inform the trial if pregnancy occurs. For the purpose of clarity, true abstinence is when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods), declaration of abstinence, withdrawal, spermicides only or lactational amenorrhoea method for the duration of a trial, are not acceptable methods of contraception)
3. Females of childbearing potential must have a negative pregnancy test seven days or fewer prior to first dose administration and must be willing to have a pregnancy test at every physical visit during the study
4. Females must not be breastfeeding
5. Known sensitivity to methylphenidate or to any of the excipients
6. History of glaucoma
7. Known phaechromocytoma
8. Planned general anaesthesia in the next nine weeks
9. During treatment with non-selective, irreversible MAO inhibitors, or within a minimum of 14 days of discontinuing those drugs
10. Clinical hyperthyroidism or thyrotoxicosis. Patients must have a thyroid function test (T4 and TSH) showing no evidence of hyperthyroidism in three months prior to first dose administration of study medication
11. Known diagnosis or history of severe depression, anorexia nervosa/anorexic disorders, suicidal tendencies, psychotic symptoms, severe mood disorders, mania, schizophrenia, psychopathic/borderline personality disorder
12. Known diagnosis or history of severe and episodic (Type 1) bipolar (affective) disorder (that is not well controlled)
13. Known pre-existing cardiovascular disorders including severe hypertension (BP >160 /100mmHg), uncontrolled heart failure, uncontrolled angina, arterial occlusive disease, haemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction (within last one year), potentially life-threatening arrhythmias and channelopathies
14. Pre-existing cerebrovascular disorders, cerebral aneurysm, vascular abnormalities including vasculitis or stroke (within last 1 year) or known high-risk factors for cerebrovascular disorders
15. Current or previous psycho-stimulant use in the last month
16. Severe anaemia (haemoglobin <80g/L)
17. Platelets <50 × 10e3/µL
18. White blood count less than 1.5 x 109/litre
19. Any evidence of severe or uncontrolled infection that in the view of the investigator makes it undesirable for the patient to participate in the trial
20. Estimated glomerular filtration rate [eGFR] <45 ml/minute per 1·73 m^2
21. ALT > 2 x ULN or bilirubin > 1.5 x ULN
22. Participating in another research study involving any investigational agents within four weeks prior to registration

23. Insufficient English language skills to understand study documentation and complete assessments
24. Current treatment with clonidine, warfarin, monoamine oxidase inhibitors or modafinil
25. History of previous or current substance or alcohol dependency within the last 1 year
26. Unable to swallow tablets/capsules
27. History of poorly controlled epilepsy, or seizures related to underlying brain tumour
28. Any other significant disease or disorder which, in the opinion of the Investigator, may put the participant at risk or affect the participant's ability to take part in the study

Patients who are still receiving tumour-directed therapies (e.g. chemotherapy or radiotherapy) will not be excluded from the study provided that the treatment is with palliative intent. Patients will be stratified by whether or not they are in receipt of disease-modifying treatment as this may be expected to affect their fatigue levels one way or another (see Section 11.6).

Previous exclusion criteria:
1. Females of childbearing potential and males must be willing to use an effective method of contraception (hormonal or barrier method of birth control; true abstinence) from the time consent is signed until 6 weeks after treatment discontinuation and inform the trial if pregnancy occurs. For the purpose of clarity, true abstinence is when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods), declaration of abstinence, withdrawal, spermicides only or lactational amenorrhoea method for the duration of a trial, are not acceptable methods of contraception)
2. Females of childbearing potential must have a negative pregnancy test within 7 days prior to being registered for trial treatment.
3. Females must not be breastfeeding.
4. Known sensitivity to methylphenidate or to any of the excipients.
5. History of glaucoma
6. Known phaechromocytoma
7. Planned general anaesthesia in the next nine weeks
8. During treatment with non-selective, irreversible monoamine oxidase (MAO) inhibitors, or within a minimum of 14 days of discontinuing those drugs
9. Hyperthyroidism or thyrotoxicosis
10. Known diagnosis or history of severe depression, anorexia nervosa/anorexic disorders, suicidal tendencies, psychotic symptoms, severe mood disorders, mania, schizophrenia, psychopathic/borderline personality disorder
11. Known diagnosis or history of severe and episodic (Type 1) Bipolar (affective) disorder (that is not well controlled)
12. Known pre-existing cardiovascular disorders including severe hypertension (BP > 160 /100mmHg), heart failure, arterial occlusive disease, angina, haemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, potentially life-threatening arrhythmias and channelopathies
13. Pre-existing cerebrovascular disorders, cerebral aneurysm, vascular abnormalities including vasculitis or stroke or known risk factors for cerebrovascular disorders
14. Current or previous psycho-stimulant use in last month
15. Severe anaemia (Haemoglobin < 80g/L)
16. Platelets < 50 × 103/μL
17. White blood count > 30 × 109/L
18. Estimated glomerular filtration rate [eGFR] < 60 ml/minute per 1·73 m^2
19. Liver function tests elevated > 3 x upper limit of normal (either ALT > 165 U/L; or AST > 144 U /L; or ALP > 345 U/L; or GGT > 144 U/L; or Bilirubin > 3.6mg/dL)
20. Currently an inpatient in a hospital or a hospice
21. Currently participating in another research study involving an investigational product

22. English not first language or unable to read English
23. Current treatment with clonidine, warfarin, monoamine oxidase inhibitors or modafinil
24. History of previous or current substance or alcohol abuse
25. Unable to swallow tablets/capsules
26. History of poorly controlled epilepsy, or seizures related to underlying brain tumour
27. Any other significant disease or disorder which, in the opinion of the Investigator, may put the participant at risk or affect the participant's ability to take part in the study

We will not exclude patients who are still receiving tumour-directed therapies (e.g. chemotherapy or radiotherapy) provided that the treatment is with palliative intent and that the expected prognosis is 2 – 12 months. We believe that to exclude such patients would make recruitment very difficult and would also mean that the study population was not representative of the broader palliative care population (in whom disease modifying treatments are frequently used up until a few weeks or months before death). Nonetheless we will stratify patients by whether or not they are in receipt of disease-modifying treatment as this may be expected to affect their fatigue levels one way or another.

Date of first enrolment
15/01/2018

Date of final enrolment
27/04/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University College London Hospital
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Martlets Hospice
Wayfield Avenue
Hove
United Kingdom
BN3 7LW

Study participating centre
Brighton General Hospital
Sussex Community NHS Foundation Trust,
Elm Grove
East Sussex
Brighton
United Kingdom
BN2 3EW

Study participating centre
Leeds Community Healthcare NHS Trust
Leeds Community, Healthcare NHS Trust
Stockdale House
8 Victoria Road
West Yorkshire
Leeds
United Kingdom
LS6 1PF

Study participating centre
Marie Curie Hospice
Hampstead
11 Lyndhurst Gardens
London
United Kingdom
NW3 5NS

Study participating centre
Pilgrims Hospices
56 London Road
Canterbury
United Kingdom
CT2 8JA

Study participating centre
Stephenson House
Central And North West, London NHS Foundation Trust
75 Hampstead Road
London
United Kingdom
NW1 2PL

Study participating centre
LOROS
Groby Road
Leicester
United Kingdom
LE3 9QE

Study participating centre
Nottinghamshire Healthcare NHS Foundation Trust
The Resource
Duncan Macmillan House
Porchester Road
Nottingham
United Kingdom
NG3 6AA

Study participating centre
Queens Medical Centre
Nottingham University Hospitals NHS Trust
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Leckhampton Court Hospice
Church Road
Leckhampton
United Kingdom
GL53 0QJ

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and analysed during the current study will be available upon request from Professor Paddy Stone, p.stone@ucl.ac.uk. IPD will be accessible after the main publications.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		10/07/2024	04/07/2024	Yes	No
HRA research summary			28/06/2023	No	No
Other files	version 13.0	01/03/2021	28/07/2023	No	No
Participant information sheet	version V4	20/07/2017	10/08/2017	No	Yes
Participant information sheet	version V4	20/07/2017	10/08/2017	No	Yes
Participant information sheet	version 13.0	01/03/2021	28/07/2023	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version V3	19/07/2017	10/08/2017	No	No
Protocol file	version 13.0	01/03/2021	27/07/2023	No	No