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Will the medication modafinil reduce post-stroke fatigue and improve quality of life of patients?

Submission date
23/05/2023

Recruitment status
Recruiting

Registration date
31/05/2023

Overall study status
Ongoing

Last Edited
09/06/2025

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The most common post-stroke symptom is 'fatigue', affecting up to 70% of stroke survivors. Stroke-related fatigue is a predictor of needing help in activities of daily living and is also associated with poor quality of life, inability to return to work and increased mortality within the first year of stroke. Most importantly, there are currently no therapies available for stroke survivors to help manage their fatigue. Modafinil is a medication to treat sleepiness due to narcolepsy, shift work sleep disorder, or obstructive sleep apnoea. A previous study tested modafinil in stroke survivors with severe persisting fatigue and found that 6 weeks of modafinil treatment reduced fatigue and improved the quality of life for the participants. This study aims to confirm the previous study results, by testing if 200mg of modafinil taken daily for 56 days can alleviate stroke-related fatigue and improve the quality of life of patients and if modafinil is safe in a large population of stroke survivors. Additionally, the study also aims to perform a short assessment of the participant's caregiver/carer to identify if modafinil treatment taken by the participant reduces the carer's burden on the caregiver.

Who can participate?
Adult stroke survivors whose stroke occurred at least three months before study entry, who self-report significant fatigue affecting their quality of life, scoring over 60 on the Multidimensional Fatigue Inventory and who have no contraindication to modafinil

What does the study involve?
Participants will attend four study visits (screening, Day 0, 28 and 56) for trial assessments. Study participants will be randomly assigned to either Modafinil (200mg daily) or Placebo Group. The treatment will last 56 days. Caregivers will also be asked to complete questionnaires at each study visit.

Suitable patients will be identified by clinical staff working in the outpatient clinics in the Stroke Services at participating sites. The process will be aided by stroke research nurses and

coordinators funded by Clinical Research Network (CRN). All research staff consenting patients will have valid GCP training. Patients meeting the inclusion criteria will be asked if they wish to participate.

Participant identification: Participants will be identified from the existing patient pools at each participating site. Stroke survivors who come into the hospital or are contacted over the phone for a follow-up will be asked if they are willing to be part of the research and are also experiencing severe fatigue. If so, their name and contact details will be recorded and passed on to a member of the research team who will approach the patient for screening and consent as well as provide detailed information about what the study involves to the participant. Patient eligibility screening will be conducted according to the protocol inclusion and exclusion criteria. Specifically, the screening requires a score of 60 or more on the MFI.

Given study participants are not eligible for enrolment till 3 months or longer following their stroke, sites participating in the study might approach their local stroke survivor registers for participants who are eligible & willing to participate in the study. e.g. bodies like the Stroke Association UK which maintain an online forum of stroke survivors who can potentially be contacted for research trials. Any proposed advertising materials will be reviewed and approved by the Ethics Committee before being implemented.

What are the possible benefits and risks of participating?
There will be no clear or definite benefit to participation in this research. However, participation will contribute to the research efforts to discover treatments that work for stroke-related fatigue. Medical treatments often cause side effects. The participant may have none, some or all of the effects listed in the participant information sheet, and they may be mild, moderate or severe. If they have any of these side effects or are worried about them, they should talk with their study doctor. The study doctor will also be looking out for side effects.

Where is the study run from?
University of Newcastle (Australia) and University of Cambridge (UK)

When is the study starting and how long is it expected to run for?
February 2017 to February 2028

Who is funding the study?
Commonwealth of Australia Medical Research Future Fund (MRFF) for Research Activities (Australian Government)

Who is the main contact?
Miss Amy Jolly, aj602@medschl.cam.ac.uk

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2019-001448-22

Integrated Research Application System (IRAS)
1004119

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
MIDAS2tele, CPMS 55358

Study information

Scientific Title
Modafinil In Debilitating Fatigue After Stroke 2 (MIDAS2 Part I and MIDAS2 Part II tele health)

Acronym
MIDAS2

Study objectives
To test the hypothesis that in stroke survivors, 200mg of modafinil taken once daily for at least 56 days significantly improves participant quality of life compared to placebo, due to the improvement of severe and persisting fatigue after stroke.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 22/09/2023, South Central - Berkshire B Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)2071048276; berkshireb.rec@hra.nhs.uk), ref: 23/SC/0191

2. approved 12/04/2018, New England Research Ethics & Governance Office (Locked Bag No 1, New Lambton, NSW 2305, Australia; +61 (0)2 49214950; HNELHD-HREC@hnehealth.nsw.gov.au), ref: 18/03/21/3.03

Study design
Randomized placebo-controlled double-blind parallel-group cross-over study

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Stroke survivors suffering from severe fatigue

Interventions

Modafinil: 200mg taken once a day for 56 days followed by an optional open-label non-randomised observational phase for 10 months. Route: oral tablet. Time of administration; Modafinil is ideally to be taken with breakfast. Treatment adherence will be monitored by drug tablet return.

Matching placebo: 200mg physically identical to modafinil tablets taken once a day for at least 56 days. Route: oral tablet. Time of administration; ideally to be taken with breakfast. Treatment adherence will be monitored by drug tablet return.

Study participants are follow-up for 12 months

Randomisation will be based on a 1:1 allocation ratio and will be performed at the individual subject-level using a centralised on-line eCRF system.

Study assessments: Assessment of fatigue and quality of life with self-reported questionnaires: Multidimensional Fatigue Inventory (MFI), 36-Item Short Form Survey (SF-36), Fatigue Severity Scale (FSS), Depressive Anxiety and Stress Scale (DASS 42) and EuroQol five dimensions questionnaire (EQ-5D). Carer burden assessment with Oberst Caregiving Burden Scale (OCBS) and Caregiver Strain Index (CS)I if applicable.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Self-reported quality of life measured using the 36-Item Short Form Survey (SF-36) at 56 days post treatment

Key secondary outcome(s))
1. Quality of life is measured using the 36-Item Short Form Survey (SF-36) at baseline, 28 days, 56 days and 12 months
2. Fatigue is measured using the Multidimensional Fatigue Inventory (MFI) at baseline, 28 days, 56 days and 12 months
3. Cognitive performance is measured using the Montreal Cognitive Assessment (MoCA) and Trail Making A and B test at baseline, 28 days, 56 days and 12 months
4. Depression, anxiety and stress is measured using a 42-item self-reported score Depressive Anxiety and Stress Scale (DASS 42) at baseline, 28 days, 56 days and 12 months
5. Generic health status is measured using the EuroQol five dimensions questionnaire (EQ-5D) at baseline, 28 days, 56 days and 12 months
6. Carer burden and concerns is measured using the Oberst Caregiving Burden Scale (OCBS) and Caregiver Strain Index (CSI) at baseline, 28 days, 56 days and 12 months
7. Degree of disability in patients who have had a stroke is measured using the Modified Ranking Scale (mRS) at baseline, 28 days, 56 days and 12 months
8. Fatigue is measured using a 9-item self-administered Fatigue Severity Scale (FSS) at baseline, 28 days, 56 days and 12 months
9. Safety is measured using the number of serious adverse events (SAEs), and the number of

study drug related rash complications at baseline, 28 days, 56 days, 3 months, 6 months and 12 months

Completion date
28/02/2028

Eligibility

Key inclusion criteria
1. 18 years of age or older
2. Have suffered a stroke (ischaemic / Haemorrhagic) at least 3 months ago
3. Have persistent self-reported fatigue with an MFI score of 60 or more
4. Modified Rankin Score (mRS) of 3 or less
5. Can speak reasonable English, understand instructions and be able to complete tests and questionnaires on their own or with minimal support
6. Able to give informed consent to participate in the study, in accordance with the ICH GCP guidelines, and local regulations, before initiating any study-related procedures

Participant type(s)
Patient, Carer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. An active, symptomatic or untreated anxiety disorder who, based on the clinical judgement of the investigator, could be prone to an exacerbation of anxiety with the use of modafinil (Note: Subjects with well-controlled anxiety who are on medication are eligible for consideration for inclusion in the trial)
2. An active, symptomatic or untreated depression who, based on the clinical judgement of the investigator could be prone to an exacerbation of depression or the development of agitation (Note: Subjects with well-controlled depression who are stable and/or have been on antidepressant medication for at least 6 months are eligible for consideration for inclusion in the trial)
3. Pre-existing dementia or other neuropsychiatric disease
4. Other diagnoses with fatigue as a known symptom e.g. chronic fatigue syndrome, multiple sclerosis, narcolepsy
5. Current or past drug abuse
6. Known contraindication to treatment with modafinil
7. Known active malignancy, intracranial tumour, subdural or epidural hematoma
8. Severe renal or hepatic impairment (GFR <15mL/min)

9. Unstable or poorly controlled epilepsy where the investigator is concerned about the potential for drug interactions. Refer to appendix 2 for specific medication guidance
10. Benzodiazepines or other hypno-sedative drugs which may interact with modafinil as per specific medication guidance provided in appendix 2
11. Clinical suspicion of sleep apnoea. If the investigator suspects on clinical grounds, that fatigue is related to sleep apnoea, an Epworth Sleepiness Scale must be undertaken. If the score is >10, overnight pulse oximetry monitoring or a sleep study must be undertaken to exclude sleep apnoea
12. Participant is receiving immunosuppressive therapy or has a known immunodeficiency state, e.g., HIV
13. Pregnant or breastfeeding women. Women of childbearing potential will need to have a negative pregnancy test at screening and should agree to using an acceptable barrier form of birth control. The effectiveness of steroidal contraceptives (contraceptive pill, implants, intrauterine devices (IUDs) or patches, etc.) may be impaired due to induction of CYP3A4/5 by modafinil. Alternative or concomitant methods of contraception are recommended for patients treated with modafinil. Acceptable methods of contraception should continue to be used for at least two months after ingestion of the final study dose.
14. Are likely unable to complete protocol requirements due to logistical factors such as inadequate Information and communication technology (ICT) capability or inability to attend for face-to-face follow-up, as assessed and confirmed by the local investigator

Date of first enrolment
06/06/2018

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
United Kingdom

England

Australia

Study participating centre
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation

University of Newcastle Australia

ROR
https://ror.org/00eae9z71

Funder(s)

Funder type
Government

Funder Name
Medical Research Future Fund

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available

IPD sharing plan summary
Not expected to be made available