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A trial investigating whether suppressing the immune system with azathioprine slows the progression of Parkinson’s disease

Submission date
14/04/2020

Recruitment status
No longer recruiting

Registration date
14/05/2020

Overall study status
Completed

Last Edited
13/02/2026

Condition category
Nervous System Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Parkinson's disease (PD) is a common neurological disorder that affects about 2% of people over 65. It is characterised by its effect on movement, but it can also cause a number of other problems including issues with mood, memory, sleep, swallowing, speech, bladder and bowel function. It is a progressive disorder: 10 years following diagnosis about two-thirds of patients have significant walking problems and half have developed dementia. There are treatments to help alleviate some of the symptoms, but no therapies to slow the underlying disease process. There is growing evidence suggesting that activation of the immune system plays a significant role in PD. This is a critical system for protecting the body from infections, but can become inappropriately activated in certain diseases, causing tissues to become inflamed and damaged. The aim of this study is to test whether suppressing the immune system with a drug called azathioprine can slow the progression of Parkinson’s disease. Azathioprine is a licenced, effective treatment for a number of inflammatory and autoimmune diseases.

Who can participate?
Patients aged over 50 with early-stage Parkinson’s disease (diagnosed within the last 3 years)

What does the study involve?
Half of the participants will receive azathioprine and half will receive placebo (dummy drug), with the treatments being allocated randomly. The azathioprine/placebo will be given in tablet form, once daily, for 1 year. The trial will be double-blinded so that neither the participants nor the researchers know who is taking the active drug. Detailed assessments will be carried out at the beginning of the trial, and at regular intervals until 6 months after the treatment is completed. The researchers will compare how measures of disease severity change over time in the azathioprine and placebo groups. They will look at markers of immune activation in the blood to assess the effect of azathioprine on immune changes in PD. Some participants will also have PET brain scans and lumbar punctures to assess immune activation within the brain and cerebrospinal fluid (these are optional assessments).

What are the possible benefits and risks of participating?
Participants will have their Parkinson's closely monitored by a specialist team over the duration of the study. Although it is possible that suppressing the immune system with azathioprine might slow down PD progression, the researchers cannot be sure of this until the end of the study, and not all participants will receive azathioprine, so taking part may not benefit participants directly. However, the results of the study will help researchers to understand more about PD and may improve the treatment of other people with this disease in the future. There are potential risks associated with taking azathioprine. These include a risk of over-suppressing the immune system and causing increased susceptibility to infections, anaemia or bleeding. There is also a risk of gastrointestinal side-effects, including nausea, and a small chance of adversely affecting liver function. However, participants will be very closely monitored with regular blood tests to mitigate risks associated with the treatment, and the dose of the drug can be reduced if it causes side effects. Participants will be asked to temporarily refrain from taking their prescribed Parkinson's medication before some of their visits. This may cause some Parkinson's related symptoms to be more noticeable, such as body stiffness, slow walking and tremor. However, participants will be able to take their medication again as soon as they have completed a physical examination. Some participants will have PET brain scans at the beginning and end of treatment, and this type of scanning involves exposure to a small amount of radioactivity. All people are at risk of developing cancer during their lifetime, and the normal risk is that this will happen to about 50% of people at some point in their life. The radioactivity exposure from taking part in the PET scans will increase the chances of this happening by a very small amount, from 50% to 50.03%. Some participants will also have a lumbar puncture before and after completing their study medication, and a possible side effect of this procedure is headache. Recent studied using modern methods suggest this occurs in around 1 in 20 people.

Where is the study run from?
The study is being coordinated by Cambridge University Hospitals NHS Trust and the University of Cambridge. Assessments will take place at the John van Geest Centre for Brain Repair and the Clinical Research Facility at the Addenbrooke's Hospital site in Cambridge (UK)

When is the study starting and how long is it expected to run for?
February 2018 to February 2024

Who is funding the study?
1. Cambridge Centre for Parkinson-Plus (UK)
2. The Cure Parkinson's Trust (UK)

Who is the main contact?
Kerry Dresser, kld57@cam.ac.uk

Contact information

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2018-003089-14

Integrated Research Application System (IRAS)
243918

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 43695, IRAS 243918

Study information

Scientific Title
AZAthioprine immunosuppression and disease modification in Parkinson’s Disease (AZA-PD): a randomised double-blind placebo-controlled phase II trial

Acronym
AZA-PD

Study objectives
There is growing evidence that implicates the immune system in both the development and progression of Parkinson’s disease (PD). Inflammation and immune activation occur both in the brain and in the periphery in PD, and a pro-inflammatory cytokine profile is associated with more rapid clinical progression. Furthermore, the risk of developing PD is related to genetic variation in immune-related genes, and reduced by the use of immunosuppressant medication.

There are treatments to help alleviate some of the symptoms of PD, but no therapies to slow the underlying disease process. The researchers propose that suppressing the peripheral immune system with azathioprine is a potential disease-modifying strategy and they are conducting a clinical trial in early PD to test this hypothesis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 06/12/2019, London Westminster Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 1048310; nrescommittee.london-westminster@nhs.net), REC ref: 19/LO/1705

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

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Parkinson's disease

Interventions

Current intervention as of 18/08/2021:
This study is designed to investigate whether azathioprine can slow the progressive nature of early PD. In order to do this, the researchers propose setting up a clinical trial, where half the participants will take azathioprine and half placebo. It will be double-blinded, so neither the researchers or participants are aware who is taking the active agent. The researchers will then compare the extent to which both groups have progressed on measures which assess the symptoms of PD. They will also investigate markers of activation of the immune system, using blood, cerebrospinal fluid and imaging, to analyse the effect of the treatment.

Potential participants will be identified from the database of attendees of the PD research clinic at the John van Geest Centre for Brain Repair, based on the inclusion and exclusion criteria of the study and using their previous assessments on the database. These patients have previously indicated (provided consent) that they are interested in being contacted about further involvement in research. The researchers aim to randomise 60 patients in total, aged 50-80 years of age and within 2 years of their diagnosis.

The potential participants will be sent the participant information sheet, and if interested, be invited to attend a screening visit. At this visit, they will first have the opportunity to raise any questions, before being asked to sign the consent form. They will then have their medical history and medication reviewed, before having some blood tests. These assessments are to ensure that they are eligible to participate in the trial, as per the inclusion/exclusion criteria. All visits will occur at either the John van Geest Centre for Brain Repair, or the Clinical Research Facility, Addenbrooke's Hospital with the exception of the imaging visits which will occur at the Wolfson Brain Imaging Centre. If they are eligible they will be given an appointment for their baseline visit, which will occur up to 42 days after screening. If during the consent process they had decided to participate in the optional parts of the study, they will also have appointments for a PET/MRI scan and/or a visit for a lumbar puncture. If so, their baseline PET scan should occur within approximately 2 weeks of screening. Following this, they will have a visit arranged for a lumbar puncture to collect CSF together with a blood sample.

During their baseline visit, they will have a clinical interview by a member of the research team. They will be assessed using the MDS-UPDRS, which scores their Parkinson’s disease related symptoms and includes a clinical examination. Part III of this assessment, the motor examination, will be videoed, which will allow for a second researcher to independently score the patient's examination. This part of the assessment will be performed first, and the appointment will be booked in the morning, as the researchers are asking patients to attend whilst OFF medication. As soon as they have completed the motor examination, they can take their medication as normal. They will then have their current concomitant medication and vital signs recorded. They will also have a cognitive assessment using the Addenbrooke’s Cognitive Examination-III and will have questionnaires administered, looking at depression, quality of life, activities of daily living and non-motor symptoms. If they had opted not to have a lumbar puncture as part of the trial, they will also have a baseline blood sample taken.

The participants will then be randomised to either azathioprine or placebo. Both the researchers and the participants will be blinded to the allocation. The treatment will be started at a low initial dose of 1 mg/kg. All participants will also be given a diary to complete. They will also be given a trial-specific information sheet, with potential side-effects and concerning symptoms to aware of. In addition, they will have the study team contact details and what to do in case of an emergency.

The participants will be asked to attend for regular monitoring visits during which they will be asked about any adverse events, their diary will be reviewed and they will have their vital signs and safety blood tests taken. The blood tests will be reviewed by an external assessor, who is unblinded. The external assessor will be an experienced clinician, who is able to make decisions regarding the test results and necessary dose changes. They will ensure the dose changes are communicated to the trial pharmacist so the new dose is dispensed and collected by the participant. The external unblinded assessor will contact the study clinician with the change in dose, who will then telephone the participant with instructions on the number of tablets to continue taking. If there are any significant concerns with the safety blood tests, the external assessor will also be able to trigger the participant withdrawal or unblinding procedure. It is important that an external assessor monitors the blood results rather than the trial team themselves, because azathioprine causes predictable changes to blood tests, and this may lead to unblinding of the trial team.

These monitoring visits will initially happen every 2 weeks. At four weeks, the dose of the trial drug will be increased, if appropriate according to the clinical profile (blood results and adverse events). Azathioprine will be increased to 2 mg/kg and the placebo dose will be doubled. The participants will then have monitoring visits every 2 weeks for a further 6 weeks, then a visit after a further 4 weeks. If they remain stable, according to the external assessor, they will then have visits every 12 weeks. Of course, if there are any problems in the interim, they can contact the trial team, who can arrange an additional visit if appropriate. If at any point the dose needs to be altered, they will have additional monitoring visits. These will be every 2 weeks for 6 weeks. Again, once the external assessor is happy that they are stable, the visits will occur every 12 weeks. To ensure that the trial team remains blinded, the placebo group will have random dose changes, with additional monitoring visits, to match the azathioprine group.

Six months after the start of the treatment, the participants will attend for a treatment midpoint visit. During this, they will have the same clinical and cognitive assessments as the baseline visit, as well as repeating the questionnaires. As before, part III MDS-UPDRS will be performed first, as the participant will be in the OFF state. It will also be videoed. They will also have their medication doses recorded and any change in their medical history. They will have a blood test taken, firstly for safety blood tests as part of the treatment monitoring protocol. However, a serum sample will also be stored for immune analysis.

They will have these assessments repeated at 12 months, as well as a blood sample for the final safety blood tests and immune analysis. At which point they will stop the treatment. During this visit, if they opted into this part of the trial, they will have a repeat lumbar puncture repeat for cerebrospinal fluid collection. Within three months of the end of treatment visit, if they opted into this part of the trial, they will have a repeat PET imaging visit.

Their final visit will occur 6 months after the end of treatment. The MDS-UPDRS III will be performed in the OFF state, and videoed. Immediately following this the participant can take their PD medication. The remainder of the MDS-UPDRS will then be performed. Their medical and medication history will be reviewed. They will complete the Addenbrookes Cognitive Examination-III. They will go through the same questionnaires related to depression, quality of life, activities of daily living and non-motor symptoms. Finally, they will have a blood sample taken.

The participants will be offered ongoing follow up through the PD research clinic at the John van Geest Centre for Brain Repair. They will remain under their standard clinical care throughout the trial.

Previous intervention:
This study is designed to investigate whether azathioprine can slow the progressive nature of early PD. In order to do this, the researchers propose setting up a clinical trial, where half the participants will take azathioprine and half placebo. It will be double-blinded, so neither the researchers or participants are aware who is taking the active agent. The researchers will then compare the extent to which both groups have progressed on measures which assess the symptoms of PD. They will also investigate markers of activation of the immune system, using blood, cerebrospinal fluid and imaging, to analyse the effect of the treatment.

Potential participants will be identified from the database of attendees of the PD research clinic at the John van Geest Centre for Brain Repair, based on the inclusion and exclusion criteria of the study and using their previous assessments on the database. These patients have previously indicated (provided consent) that they are interested in being contacted about further involvement in research. The researchers aim to randomise 60 patients in total, aged 50-80 years of age and within 2 years of their diagnosis. They are looking to recruit a cohort of patients who have a poor prognosis; greater than 50% chance dementia, postural instability or death within 5 years, based on a validated predictive calculator.

The potential participants will be sent the participant information sheet, and if interested, be invited to attend a screening visit. At this visit, they will first have the opportunity to raise any questions, before being asked to sign the consent form. They will then have their medical history and medication reviewed, before having some blood tests. These assessments are to ensure that they are eligible to participate in the trial, as per the inclusion/exclusion criteria. All visits will occur at either the John van Geest Centre for Brain Repair, or the Clinical Research Facility, Addenbrooke's Hospital with the exception of the imaging visits which will occur at the Wolfson Brain Imaging Centre. If they are eligible they will be given an appointment for their baseline visit, which will occur up to 42 days after screening. If during the consent process they had decided to participate in the optional parts of the study, they will also have appointments for a PET/MRI scan and/or a visit for a lumbar puncture. If so, their baseline PET scan should occur within approximately 2 weeks of screening. Following this, they will have a visit arranged for a lumbar puncture to collect CSF together with a blood sample.

During their baseline visit, they will have a clinical interview by a member of the research team. They will be assessed using the MDS-UPDRS, which scores their Parkinson’s disease related symptoms and includes a clinical examination. Part III of this assessment, the motor examination, will be videoed, which will allow for a second researcher to independently score the patient's examination. This part of the assessment will be performed first, and the appointment will be booked in the morning, as the researchers are asking patients to attend whilst OFF medication. As soon as they have completed the motor examination, they can take their medication as normal. They will then have their current concomitant medication and vital signs recorded. They will also have a cognitive assessment using the Addenbrooke’s Cognitive Examination-III and will have questionnaires administered, looking at depression, quality of life, activities of daily living and non-motor symptoms. If they had opted not to have a lumbar puncture as part of the trial, they will also have a baseline blood sample taken.

The participants will then be randomised to either azathioprine or placebo. Both the researchers and the participants will be blinded to the allocation. The treatment will be started at a low initial dose of 1 mg/kg. All participants will also be given a diary to complete. They will also be

given a trial-specific information sheet, with potential side-effects and concerning symptoms to aware of. In addition, they will have the study team contact details and what to do in case of an emergency.

The participants will be asked to attend for regular monitoring visits during which they will be asked about any adverse events, their diary will be reviewed and they will have their vital signs and safety blood tests taken. The blood tests will be reviewed by an external assessor, who is unblinded. The external assessor will be an experienced clinician, who is able to make decisions regarding the test results and necessary dose changes. They will ensure the dose changes are communicated to the trial pharmacist so the new dose is dispensed and collected by the participant. The external unblinded assessor will contact the study clinician with the change in dose, who will then telephone the participant with instructions on the number of tablets to continue taking. If there are any significant concerns with the safety blood tests, the external assessor will also be able to trigger the participant withdrawal or unblinding procedure. It is important that an external assessor monitors the blood results rather than the trial team themselves, because azathioprine causes predictable changes to blood tests, and this may lead to unblinding of the trial team.

These monitoring visits will initially happen every 2 weeks. At four weeks, the dose of the trial drug will be increased, if appropriate according to the clinical profile (blood results and adverse events). Azathioprine will be increased to 2 mg/kg and the placebo dose will be doubled. The participants will then have monitoring visits every 2 weeks for a further 6 weeks, then a visit after a further 4 weeks. If they remain stable, according to the external assessor, they will then have visits every 12 weeks. Of course, if there are any problems in the interim, they can contact the trial team, who can arrange an additional visit if appropriate. If at any point the dose needs to be altered, they will have additional monitoring visits. These will be every 2 weeks for 6 weeks. Again, once the external assessor is happy that they are stable, the visits will occur every 12 weeks. To ensure that the trial team remains blinded, the placebo group will have random dose changes, with additional monitoring visits, to match the azathioprine group.

Six months after the start of the treatment, the participants will attend for a treatment midpoint visit. During this, they will have the same clinical and cognitive assessments as the baseline visit, as well as repeating the questionnaires. As before, part III MDS-UPDRS will be performed first, as the participant will be in the OFF state. It will also be videoed. They will also have their medication doses recorded and any change in their medical history. They will have a blood test taken, firstly for safety blood tests as part of the treatment monitoring protocol. However, a serum sample will also be stored for immune analysis.

They will have these assessments repeated at 12 months, as well as a blood sample for the final safety blood tests and immune analysis. At which point they will stop the treatment. During this visit, if they opted into this part of the trial, they will have a repeat lumbar puncture repeat for cerebrospinal fluid collection. Within three months of the end of treatment visit, if they opted into this part of the trial, they will have a repeat PET imaging visit.

Their final visit will occur 6 months after the end of treatment. The MDS-UPDRS III will be performed in the OFF state, and videoed. Immediately following this the participant can take their PD medication. The remainder of the MDS-UPDRS will then be performed. Their medical and medication history will be reviewed. They will complete the Addenbrookes Cognitive Examination-III. They will go through the same questionnaires related to depression, quality of life, activities of daily living and non-motor symptoms. Finally, they will have a blood sample taken.

The participants will be offered ongoing follow up through the PD research clinic at the John van Geest Centre for Brain Repair. They will remain under their standard clinical care throughout the trial.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Axial and gait symptoms measured using MDS-UPDRS gait/axial score in the OFF state at 12 months. This score is a sum of the points from the following sections of MDS-UPDRS part III (motor examination):
3.1. Speech
3.2. Facial expression
3.9. Rising from a chair
3.10. Gait
3.12. Postural stability
3.13. Posture
3.14. Body bradykinesia

Key secondary outcome(s))
Exploratory outcomes:
1. Axial and gait symptoms measured using MDS-UPDRS gait/axial score in OFF state at 18 months (6 months post treatment cessation)
2. Parkinson’s disease severity measured using MDS-UPDRS parts I, II and III in OFF state at 12 and 18 months
3. Bradykinesia and tremor measured using electromagnetic sensor (EMS) measurements whilst performing MDS-UPDRS tremor and bradykinesia assessments at 12 and 18 months
4. Proportion of patients developing postural instability measured using Hoehn and Yahr stage 3 or greater at 12 and 18 months
5. Global cognition measured using Addenbrooke's Cognitive Examination III (ACE-III) at 12 and 18 months
6. Patient-reported quality of life measured using Parkinson's disease questionnaire-39 (PDQ-39) at 12 and 18 months
7. Non-motor symptoms measured using non-motor symptom scale (NMSS) at 12 and 18 months
8. Parkinson’s disease treatment measured using the dose of symptomatic dopaminergic therapy (Levodopa-Equivalent Daily Dose [LEDD]) at 12 and 18 months
9. Safety and tolerability of azathioprine assessed by the number of adverse events (AEs) recorded during the 12-month treatment period
10. Total lymphocyte count measured using a blood test (full blood count) at 6, 12 and 18 months
11. Serum IgG levels measured using a blood test (immunoglobulins) at 6, 12 and 18 months
12. Levels of serum immune markers measured using cytokine immunoassays and immunophenotyping at 6, 12 and 18 months and CSF immune markers at 12 months
13. Microglial activation measured using [11C]-PK11195 PET non-dissociable binding potential (BPND) in subcortical and cortical regions of interest at 12 months

Completion date
28/02/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 18/08/2021:
1. Capable of giving signed informed consent which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol
2. Aged between 50 and 80 years
3. Fluent English speaker, as assessed by the trial team during the screening assessment
4. Diagnosis of PD according to UK Parkinson's Disease Society (UKPDS) Brain Bank Criteria, though a positive family history of PD will not be used to exclude participants
5. Disease duration <3 years
6. Adequate organ and marrow function, as defined below (measured within 42 days of first dose of trial medication):
6.1. Haemoglobin (Hb) ≥110 g/L
6.2. Platelet count ≥130 x 10(9)/L
6.3. Neutrophil count ≥1.5 x 10(9)/L
6.4. Renal function - creatinine clearance ≥ 50mL/min
6.5. Hepatic function - Alanine aminotransferase (ALT) ≤2x the institutional upper limit of normal (ULN) and total bilirubin ≤2x ULN

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Previous inclusion criteria:
1. Be capable of giving signed informed consent which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol
2. Aged 50 years or over
3. Be a fluent English speaker
4. Have a diagnosis of PD according to UKPDS Brain Bank Criteria
5. Have a disease duration of < 3 years
6. Have a probability of poor outcome (postural instability/dementia/death) at 5 years from diagnosis > = 50%
7. Have adequate organ and marrow function, as defined below (measured within 42 days of first dose of trial medication):
7.1. Haemoglobin > = 110 g/L
7.2. Platelet count > = 130 x 10(9)/L
7.3. Neutrophil count > = 1.5 x 10(9)/L
7.4. Renal function- creatinine clearance > = 50mL/min
7.5. Hepatic function- alanine aminotransferase (ALT) < = 2 times the institutional upper limit of normal (ULN) and total bilirubin < = 2 times the ULN

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
50 years

Upper age limit
80 years

Sex
All

Total final enrolment
67

Key exclusion criteria
Current exclusion criteria as of 18/08/2021:
1. Any use of immunomodulatory drugs such as azathioprine, mycophenolate, methotrexate, ciclosporin, cyclophosphamide within the 12 months prior to screening
2. Any previous use of rituximab or alemtuzumab at any time
3. Treatment with oral corticosteroids for greater than 2 weeks within the 12 months prior to screening, or any oral steroid use in 3 months prior to screening
4. Regular use of NSAIDs including aspirin >75 mg, naproxen, ibuprofen, meloxicam on more than 2 days per week
5. Known inflammatory or autoimmune disease
6. Chronic or latent infection
7. Active infection requiring the use of parenteral antimicrobial agents within 2 months prior to the first dose of trial treatment
8. Skin malignancy or solid organ malignancy within the last 5 years prior to screening assessment
9. Current or previous haematological malignancy
10. Positive test for human immunodeficiency virus (HIV) or hepatitis
11. The inability to take or swallow oral medication
12. Dementia according to Movement Disorder Society (MDS) dementia criteria
13. Thiopurine methyltransferase (TPMT) deficiency <10 pmol/h/mg Hb
14. Lack of immunity to varicella zoster virus (VZV)
15. Negative Epstein-Barr virus (EBV) IgG
16. Chronic liver disease
17. Renal impairment - creatinine clearance <50 mL/min
18. Concomitant use of allopurinol (increases risk of myelotoxicity)
19. Any concurrent medical or psychiatric condition or disease (e.g. active systemic infection, uncontrolled diabetes, acute diffuse infiltrative pulmonary disease) that is likely to interfere with the trial procedures or results, or that in the opinion of the investigator, would constitute a hazard for participating in this trial
20. Receipt of live, attenuated vaccine within the last 30 days prior to the screening assessment. Note: enrolled patients should not receive live, attenuated vaccine while receiving azathioprine nor within 30 days of last dose of azathioprine
21. Women of childbearing potential. Female patients must be surgically sterile or be postmenopausal. Postmenopausal is defined as spontaneous cessation of regular menses for at least 12 consecutive months or follicle-stimulating hormone (FSH) blood levels in the testing laboratory’s respective postmenopausal range with no alternative pathological or physiological cause.
22. Male patients must be surgically sterile or must agree to use effective contraception during

the period of therapy and for 6 months after completion of trial drug
23. Known hypersensitivity to azathioprine or its excipients
24. Received an investigational drug (including investigational vaccines) or used an invasive investigational medical device within 4 weeks before the screening assessment or is currently enrolled in an interventional investigational trial
25. High risk of severe COVID-19 on the basis of co-morbidity/frailty, on the judgement of the investigators (applicable during the COVID-19 pandemic).

Previous exclusion criteria:
1. Any use of immunomodulatory drugs such as azathioprine, mycophenolate, methotrexate, ciclosporin, cyclophosphamide within the last 12 months
2. Any previous use of rituximab or alemtuzumab
3. Previous treatment with corticosteroids for greater than 2 weeks, or any steroid use in the last 3 months
4. Regular use of non-steroidal anti-inflammatory drugs including aspirin > 75 mg, naproxen, ibuprofen, meloxicam on more than 2 days per week.
5. Known inflammatory or autoimmune disease
6. Chronic or latent infection
7. Active infection requiring the use of parenteral antimicrobial agents within 2 months prior to the first dose of study treatment.
8. Skin malignancy or solid organ malignancy within the last 5 years.
9. Current or previous haematological malignancy
10. Positive test for HIV or hepatitis
11. The inability to take or swallow oral medication
12. Dementia according to Movement Disorder Society dementia criteria
13. Thiopurine methyltransferase (TPMT) deficiency < 10 pmol/h/mg Hb
14. Lack of immunity to VZV
15. Negative EBV IgG
16. Chronic liver disease
17. Renal impairment - creatinine clearance < 50 mL/min
18. Concomitant use of allopurinol (increases risk of myelotoxicity)
19. Any concurrent medical or psychiatric condition or disease (e.g. active systemic infection, uncontrolled diabetes, acute diffuse infiltrative pulmonary disease) that is likely to interfere with the study procedures or results, or that in the opinion of the investigator, would constitute a hazard for participating in this study.
20. Receipt of live, attenuated vaccine within the last 30 days. Note: enrolled patients should not receive live, attenuated vaccine while receiving azathioprine nor within 30 days of the last dose of azathioprine
21. Women of childbearing potential. Female patients must be surgically sterile or be postmenopausal. Postmenopausal is defined as spontaneous cessation of regular menses for at least 12 consecutive months or follicle-stimulating hormone (FSH) blood levels in the testing laboratory’s respective postmenopausal range with no alternative pathological or physiological cause.
22. Male patients must be surgically sterile or must agree to use effective contraception during the period of therapy and for 6 months after completion of trial drug
23. Known hypersensitivity to azathioprine or its excipients
24. Received an investigational drug (including investigational vaccines) or used an invasive investigational medical device within 4 weeks before treatment protocol registration or is currently enrolled in an interventional investigational study

Date of first enrolment
30/03/2021

Date of final enrolment
30/07/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrookes Hospital
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Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Charity

Funder Name
Cambridge Centre for Parkinson-Plus

Funder Name
The Cure Parkinson’s Trust

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during the current trial can be made available upon request to the AZA-PD Trial Management Group (TMG), or the Chief Investigator where the TMG is not available. Requests can be made to cuh.neurosciencecctu@nhs.net. Requests for access to the datasets will be considered after at least 6 months following publication of the trial results, until 10 years following the initial publication. All research data leaving Cambridge University Hospitals NHS Trust/Cambridge University will be de-identified participant data (IPD). Consent to share IPD with investigators who are undertaking similar research projects is sought from participants during the informed consent process. Investigators will be required to have ethical approval for their project prior to the sharing of any IPD.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/01/2026	17/12/2025	Yes	No
Protocol article	protocol	23/11/2020	04/01/2021	Yes	No
HRA research summary			28/06/2023	No	No