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# A clinical trial to explore the potential of ondansetron for treating hallucinations in people with Parkinson's disease

**Submission date**
10/10/2019

**Recruitment status**
Recruiting

**Registration date**
05/02/2020

**Overall study status**
Ongoing

**Last Edited**
13/11/2025

**Condition category**
Nervous System Diseases

[X] 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
Visual hallucinations (seeing things that do not exist) occur in 75% of people with Parkinson's across the illness course, are often highly distressing, have a significant impact on quality of life, and are associated with dementia and earlier care home placement. NHS treatment options are currently limited to medications known as antipsychotics that are associated with significant side-effects, including sedation, falls, worsening of Parkinson's symptoms (tremor, movement co-ordination) and memory problems. Usual treatment involves quetiapine, as it is safer than other antipsychotic drugs, but of questionable effectiveness, or clozapine, which is effective but not feasible for use outside specialist units due to safety monitoring requirements. Pimavanserin, is a newly developed drug that has shown modest treatment effects, but is highly expensive, and not licensed for use in the UK. Findings treatments that are safe, effective, cost effective and practical for use in NHS clinics is a priority. Ondansetron, a drug used to treat post-operative nausea and vomiting, was identified as a highly promising candidate treatment for Parkinson's hallucinations in the early 1990s, when 16 people with Parkinson's and persistent severe visual hallucinations improved with ondansetron (12-24mg daily), 14 with complete resolution of symptoms, with no worsening of Parkinson's symptoms, memory or functional ability. Further studies were not carried out at the time because the drug was then extremely expensive. Costs are now much less (equivalent to usual treatment) and a larger trial in people with Parkinson's is feasible, timely and highly necessary

Who can participate?
People with Parkinson's, aged over 55 years, who are experiencing hallucinations at least weekly, at a point when other approaches to treatment (altering lighting, reducing Parkinson's medication) have failed

What does the study involve?
Those taking part will be allocated (randomly via a computerized system) to receive drug or placebo and neither the prescribing clinicians or participants will know which treatment they are taking. The dose of the study drug will increase from one (8mg or placebo) tablet, to a maximum of 3 tablets over the first 6 weeks, guided by telephone monitoring of side effects and safety (2

and 4 weeks). Treatment will then continue for a further 6 weeks. Usual treatment (quetiapine) will be available to all participants if required, to ensure that distressing symptoms are not left untreated. Face to face assessments and blood sampling will be carried out after 6 and 12 weeks treatment, and over the telephone after treatment has completed (16 and 24 weeks). Recruitment will take place over 2 years in 15-20 NHS clinics, supported by local Research Networks and Parkinson's UK. It will also be possible for participants to refer themselves to the study. Agreed recruitment targets are 5 participants per site in the first year, and progress will be assessed 9 months into recruitment by the Trial Management Group, to identify barriers to recruitment or retention to the study and ensure that they are addressed in a timely way. There will be focus group representation on biannual trial committees that will monitor progress towards recruitment targets, safety and data management throughout the study

What are the possible benefits and risks of participating?
Ondansetron is licensed for short term use as an anti-emetic and has undergone extensive safety testing for this indication. Any observed treatment benefits are likely to outweigh the risks. There is no guarantee of any direct benefit to you as a result of participating in this research study but ondansetron may help to treat visual hallucinations and may help reduce delusions associated with Parkinson's disease. Your participation may provide information useful to the understanding of ondansetron and Parkinson's disease. Constipation, which is common in people with Parkinson's, is a known side effect of ondansetron and a dose titration phase will be used to reduce the burden of possible side effects

Where is the study run from?
University College London, UK

When is the study starting and how long is it expected to run for?
April 2020 to December 2027

Who is funding the study?
Parkinson's UK

Who is the main contact?
Dr Olga Zubko
o.zubko@ucl.ac.uk

# Contact information

### Type(s)
Public

### Contact name
Dr Olga Zubko

### Contact details
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# Additional identifiers

### Clinical Trials Information System (CTIS)
2019-003962-41

### Integrated Research Application System (IRAS)
266504

### ClinicalTrials.gov (NCT)
NCT04167813

### Protocol serial number
17/0909, IRAS 266504

# Study information

### Scientific Title
Trial of Ondansetron as a Parkinson’s HAllucinations Treatment

### Acronym
TOP HAT

### Study objectives
The study will test the hypothesis that flexibly dosed ondansetron (8-24mg/day) will have a clinically meaningful treatment effect on visual hallucinations in people with Parkinson’s, without worsening motor or cognitive symptoms.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 03/02/2020, East of England - Cambridge East Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 2071048265; cambridgeeast.rec@hra.nhs.uk), ref: 19/EE/0377

### Study design
Double-blind individually randomized placebo-controlled parallel-group flexible-dose trial

### Primary study design
Interventional

### Study type(s)
Treatment

### Health condition(s) or problem(s) studied
Parkinson's hallucinations

## Interventions
The intervention will consist of flexible dosing of ondansetron/placebo (8-24mg/day) as a treatment for Parkinson's hallucinations, with a 12-week primary outcome and follow-up to 24 weeks. The treatment dose will increase from a single daily 8 mg tablet (AM) (weeks 1 and 2), to 16 mg/day (8 mg twice daily) (weeks 3 and 4), with a further increase to 24 mg/day (8 mg AM, 16 mg PM) (weeks 5 and 6).

The study will recruit people with Parkinson's, aged over 55 years, who are experiencing hallucinations at least weekly, at a point when other approaches to treatment (altering lighting, reducing Parkinson's medication) have failed. Those taking part will be allocated (randomly via a computerized system) to receive drug or placebo and neither the prescribing clinicians or participants will know which treatment they are taking. The dose of the study drug will increase from one (8 mg or placebo) tablet, to a maximum of 3 tablets over the first 6 weeks, guided by telephone monitoring of side effects and safety (2 and 4 weeks). Treatment will then continue for a further 6 weeks. Usual treatment (quetiapine) will be available to all participants if required, to ensure that distressing symptoms are not left untreated. Face to face assessments and blood sampling will be carried out after 6 and 12 weeks treatment, and over the telephone after treatment has completed (16 and 24 weeks). Recruitment will take place over 2 years in 15-20 NHS clinics, supported by local Research Networks and Parkinson's UK. It will also be possible for participants to refer themselves to the study. Agreed recruitment targets are 5 participants per site in the first year, and progress will be assessed 9 months into recruitment by the Trial Management Group, to identify barriers to recruitment or retention to the study and ensure that they are addressed in a timely way. There will be focus group representation on biannual trial committees that will monitor progress towards recruitment targets, safety and data management throughout the study.

## Intervention Type
Drug

## Phase
Phase II

## Drug/device/biological/vaccine name(s)
Ondansetron

## Primary outcome(s)
Visual Hallucinations measured using SAPS-H (12 weeks)

## Key secondary outcome(s))
1. Visual hallucinations measured using SAPS-H (2, 4, 6, 12, 18, 24 weeks)
2. Delusions measured using SAPS-D (2, 4, 6, 12, 18, 24 weeks)
3. Global Severity (Impact) of symptoms measured using CGI-S (2, 4, 6, 12, 18, 24 weeks)
4. Hallucinations measured using UM-PDHQ (12 weeks)
5. Non-motor symptoms measured using NMSS (6, 12, 18, 24 weeks)
6. Proportion receiving quetiapine rescue medication at end of treatment (12 weeks) and follow-up (24 weeks) periods
7. Health-related quality of life measured using Euro-QoL, EQ-5D (6, 12, 18, 24 weeks) Parkinson's symptoms (tremor, rigidity) UPDRS III (6, 12 weeks)
8. Cognition measured using sMMSE (12 weeks)
9. ECG changes measured using QTc interval (6 weeks)

10. Tolerability measured using adverse event checklist (2, 4, 6, 12, 18, 24 weeks)
11. Pharmacokinetics measured using Venous blood drug concentration (6, 12 weeks)
12. Visual information processing measured using HVOT (12 weeks)

### Completion date
31/12/2027

## Eligibility

### Key inclusion criteria
1. Aged over 55 years
2. Meet Brain Bank criteria for Parkinson's disease
3. Visual hallucinations have been present at least weekly in the month before screening and are moderately severe
4. On a stable dose of anti-Parkinson's medication, cholinesterase inhibitor or memantine for at least 28 days
5. Capacity to give informed consent or (if lacking) caregiver or other legal representative able to give consent
6. Pre-menopausal women, and men whose partners are of child bearing potential who agree to use effective contraception during the trial treatment period

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Mixed

### Lower age limit
55 years

### Upper age limit
100 years

### Sex
All

### Total final enrolment
0

### Key exclusion criteria
1. Bradycardia (<50 bpm) (rescreen if reversible)
2. Congenital long QTc syndrome or presence of clinically significant prolongation of QTc (>460 ms for men or >470 ms for women) on ECG screening.
3. Severe hepatic failure (bilirubin >50 micromole/L)
4. Prescribed any antipsychotic medication in the past 2 weeks
5. Prescribed apomorphine
6. Prescribed tropisetron, granisetron, dolasetron

7. History of hypersensitivity to ondansetron and its excipients (or those of placebo) or drugs listed in 6
8. Participation in another Clinical Trial of an Investigational Medicinal Product (IMP) in the previous 28 days

### Date of first enrolment
01/04/2020

### Date of final enrolment
31/07/2026

## Locations

### Countries of recruitment
United Kingdom

England

Wales

### Study participating centre
**Leonard Wolfson Experimental Neurology Centre**
Gower St
Bloomsbury
Epsom
England
WC1N 3BG

### Study participating centre
**Salford Royal NHS Foundation Trust**
Stott Lane
Manchester
England
M6 8HD

### Study participating centre
**Pennine Acute Hospitals NHS Trust**
Fairfield General Hospital
Rochdale Old Road
Bury
England
BL9 7TD

**Study participating centre**
**Cambridge University Hospitals NHS Foundation Trust**
Hills Road
Cambridge NO COUNTRY SPECIFIED, assuming England
England
CBQ 0QQ

**Study participating centre**
**Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust**
Castle Ln E
Bournemouth
England
BH7 7DW

**Study participating centre**
**Northumbria Healthcare NHS Foundation Trust**
Unit 7-8 Silver Fox Way Cobalt Business Park
Newcastle upon Tyne
England
NE12 8EW

**Study participating centre**
**Royal Devon and Exeter NHS Trust**
Barrack Rd
Exeter
England
EX2 5DW

**Study participating centre**
**Royal United Hospitals Bath**
Combe Park
Bath
England
BA1 3NG

**Study participating centre**
**Wrexham Maelor Hospital**
Croesnewydd Road
Wrexham
Wales
LL137TD

**Study participating centre**
**Ysbyty Gwynedd**
-
Bangor
Wales
LL57 2PW

**Study participating centre**
**LLandudno Hospital**
Hospital Rd
Llandudno
Wales
LL30 1LB

**Study participating centre**
**Holyhead Hospital**
Penrhos Beach Rd
Anglesey
Holyhead
Wales
LL65 2QA

# Sponsor information

**Organisation**
PRIMENT CTU

# Funder(s)

**Funder type**
Charity

**Funder Name**
Parkinson's UK

**Alternative Name(s)**
Parkinson's Disease Society

### Funding Body Type
Private sector organisation

### Funding Body Subtype
Associations and societies (private and public)

### Location
United Kingdom

## Results and Publications

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary
Data sharing statement to be made available at a later date

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| HRA research summary | | | 28/06/2023 | No | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |