ISRCTN63917405 https://doi.org/10.1186/ISRCTN63917405

Clinical and cost-effectiveness of an aripiprazole and sertraline drug combination in comparison with the drug quetiapine for the treatment of bipolar depression

Submission date
30/06/2023

Recruitment status
Recruiting

Registration date
23/11/2023

Overall study status
Ongoing

Last Edited
21/11/2025

Condition category
Mental and Behavioural Disorders

[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
Bipolar disorder (BP) affects more than 1 person in 100, negatively impacts people's lives and places a tremendous strain on caregivers, the NHS and society. It causes earlier-than-expected death, including by suicide. Depression is common in BP ("bipolar depression"). People with unipolar depression usually improve with a standard antidepressant or talking therapy, but only specialist psychological treatments are recommended in BP. These are not widely available and have not convincingly been shown to treat bipolar depression. Similarly, in BP, antidepressant drugs, when taken by themselves, show no therapeutic value. In light of this, the National Institute of Clinical Excellence (NICE) largely recommends treatment with so-called 'antipsychotic' drugs. These are often poorly tolerated causing sedation, weight gain, sleep disturbance and diabetes. Most current treatment options are also only recommended to be started by psychiatrists. So, additional treatment options are needed and this has been identified by the James Lind Alliance (JLA) as a priority for patients. A previous small trial indicated a combination of the antipsychotic aripiprazole with an antidepressant may be effective in bipolar depression, with a reduced burden of side effects compared to current treatments. It is time now for a large trial to see if this combination works.

Who can participate?
Adults aged over 18 years old with BP from primary and secondary care services

What does the study involve?
Participants will be randomised to receive an aripiprazole/sertraline combination or quetiapine. The participants will be followed up for 24 weeks using questionnaires to examine any longer-term benefits on depressive symptoms, quality of life and costs. 10 NHS trusts will take part in the study.

What are the possible benefits and risks of participating?
The study team think there are minimal risks to being part of this study as all the medications

are currently used in the NHS. However, all medications carry some risks. Some of the common side effects of these drugs may include headaches, weight gain, feeling sleepy and nausea. Participants will be in regular contact with study central research assistants and asked to report side effects they may experience via ePRO and discuss these with an investigator at their participating site. If at any point during the study, the investigator thinks it would be beneficial for a participant to stop taking part, they will be withdrawn.

Participants will also be required to answer a large number of questionnaires throughout the study, but this was acceptable in the similar PAX-BD study and has been reviewed by our PPI group.

Where is the study run from?
St Nicholas Hospital (UK)

When is the study starting and how long is it expected to run for?
September 2022 to December 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) Programme

Who is the main contact?
ASCEND study team, ASCEND@newcastle.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

Contact name
Dr Stuart Watson

Contact details
St Nicholas Hospital
Newcastle upon Tyne
United Kingdom
NE3 3XT
+44(0)191 2468606
stuart.watson@newcastle.ac.uk

Type(s)
Public

Contact name
Dr ASCEnD Trial Management Team

Contact details
Newcastle Clinical Trials Unit
1-4 Claremont Terrace
Newcastle University
Newcastle upon Tyne

United Kingdom
NE2 4AE
None provided
ASCEND@newcastle.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1007468

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
RES-20-32, IRAS 1007468, CPMS 57451

Study information

Scientific Title
Aripiprazole/sertraline combination: clinical and cost-effectiveness in comparison with quetiapine for the treatment of bipolar depression. An open label randomised controlled trial

Acronym
ASCEnD

Study objectives
The primary objective of the trial is to test the hypothesis that improvement in depression will be greater in participants randomised to aripiprazole/sertraline combination than those randomised to quetiapine.

The study's secondary objectives will compare the impact of aripiprazole/sertraline combination versus quetiapine over a 24-week follow up period. This will be achieved by asking participants to complete questionnaires to assess changes in their symptoms, overall wellbeing, their health related quality of life and assessing the cost-effectiveness of these treatments.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 22/11/2023, North East - Newcastle & North Tyneside 1 Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8384; newcastlenorthtyneside1.rec@hra.nhs.uk), ref: 23/NE/0132

Study design
Randomized active-controlled open-label parallel-group study

Primary study design

Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Bipolar depression

Interventions
The ASCEnD trial is a prospective, two-arm, open-label, superiority, individually 1:1 randomised, controlled, pragmatic, parallel-group, type A open-label clinical trial. It aims to determine whether a sertraline/aripiprazole medication combination is an effective treatment for bipolar depression. The trial will be carried out at UK sites including primary, secondary and tertiary care mental health services. A target of 270 patients will be randomised (1:1 ratio) to receive either sertraline/aripiprazole combination or quetiapine. The effectiveness of sertraline/aripiprazole combination in reducing depressive symptoms will be assessed 12-16 weeks after randomisation. Patients and their main informal carers will continue to be followed up for 24 weeks. Over this period, the cost-effectiveness and the effect of the sertraline/aripiprazole combination on symptoms of depression, anxiety and mania will be assessed. Assessments will be completed by participants and their main informal carer online using electronic Patient Reported Outcomes (ePRO) or, for participants where this is not possible, via telephone or videoconference with a cRA.

The study will recruit patients with a pre-existing diagnosis of bipolar disorder, as well as those whose bipolar disorder is not yet recognised. The Clinical Research Networks (CRNs) will support recruitment which will be via a number of routes. The eligibility criteria for this trial are pragmatic, in line with UK clinical practice. There is no upper or lower limit of bipolar disorder treatment resistance, duration of current depressive episode, time since initial symptoms or time since the diagnosis of bipolar disorder. Patients will not be excluded if they are receiving, planning to receive or have recently received psychological or digital therapies.

Patients must fulfil all of the following criteria to progress to randomisation: aged 18 or over at the point of consent; able to provide written informed consent; A current (i.e., within 7 days) DSM-5-TR confirmed diagnosis of a major depressive episode within bipolar disorder, be confirmed using the SCID-5-RV; a current (i.e., within 7 days) QIDS-SR >10; clinical uncertainty regarding the next course of treatment and judgement that the sertraline/aripiprazole combination and quetiapine treatment arms are both clinically appropriate and represent equipoise., and in the opinion of the clinician, the participant is able to follow trial prescription instructions, complete weekly questionnaires and engage in weekly telephone calls with the cRAs throughout the 24 weeks follow up period of the trial. Any of the following criteria prevent progression to randomisation: currently participating in any other interventional clinical trial that may affect the outcome of ASCEnD; DSM-5-TR-defined severe substance use disorder; any known contraindications to aripiprazole, sertraline or quetiapine; and currently pregnant, planning to become pregnant during the trial and/or breastfeeding.

The electronic data capture system used in ASCEnD is Red Pill. ePRO is a function of the data capture system that allows participants to enter questionnaire responses directly into the clinical trial database. Participants will be encouraged to complete questionnaires weekly via ePRO throughout the study via email or text prompts. If a participant does not have access to the internet or is otherwise unable to enter data directly into ePRO, this process will be supported by the cRAs who will complete the questionnaires by telephone or videoconference

with the participant and enter data on their behalf directly into the appropriate electronic Case Report Forms (eCRFs).

The screening and consent appointment will be conducted by the site PI, or delegate, who is a GMC registered doctor. The site PI, or delegate, will discuss the trial with the potential participant, encourage them to ask questions about the trial and inform them of their right to withdraw at any time without any impact on the standard of care they will receive or their legal rights. The appointment serves to (i) Enable the potential participant to make an informed and capacious decision about whether to participate in the study. (ii) Formally take and record study consent. (iii) Confirm all eligibility criteria for study participation are met. This includes completion of the SCID-5-RV diagnostic interview and QIDS-SR on paper (a paper study questionnaire booklet is available), and entry of this information directly into the appropriate eCRFs by delegated site staff. (iv) Collect relevant study information including method of identification, current concomitant medications, recent (within 6 months) current and planned psychological therapy, medical history (time since diagnosis) and demographic details (including initials, age, sex at birth, gender, highest level of education, family status (single/divorced /married), ethnicity and post-code), and entry of this information directly into the appropriate eCRFs by delegated site staff. (v) Provide the potential participant with access to ePRO and support with completion and use of the system. Participants will be prompted after their first login to change their password to something that only they know.

Consent for trial participation must be sought by the site PI, or delegate, who is a GMC registered doctor. Eligibility for the ASCEnD trial must be assessed by a GMC-registered doctor after receiving written informed consent from a patient to take part in the study. Once a participant is confirmed as eligible to take part in the study, a baseline appointment will be arranged. The screening and baseline appointments are likely to occur during the same visit. Baseline measures will be completed on paper.

Eligible participants will be randomised in a 1:1 ratio to aripiprazole/sertraline combination or quetiapine. Randomisation will incorporate block stratification using three variables (being in mental health secondary care services at screening (y/n), being prescribed antidepressants at screening (y/n), and being prescribed an antipsychotic at screening (y/n)). Randomisation will be conducted by a delegated and trained member of the site team at each site using Red Pill (a central, secure, 24-hour web-based randomisation system, which is owned by Sealed Envelope™). Randomisation should take place as soon as possible and no more than one week after a participant has been confirmed as eligible.

Prescriptions for study medications will be written by the participant's clinical team. The study does not mandate the use of specific medication dosages or dose escalation procedures. Instead, clinicians are encouraged to use their judgement in accordance with clinical guidelines and the BNF dose schedule. Dosage decisions and decisions regarding the ongoing use of study medications taken during the study remain the responsibility of the prescribing clinician but are informed by a participant's weekly clinical scale scores and reported side effects. Further guidance is provided in Appendix 1 of the protocol. Participants who discontinue trial medication will be encouraged to remain in the trial and to continue to provide outcome data. ASCEnD has clear progression criteria and the progress of the study will be continually monitored by the study team and Funder.

All participants are followed up for 24 weeks while taking trial medication, with weekly measures completed through to week 24, with additional measures completed at weeks 4, 14 and 24. After 24 weeks of follow-up, participants who are being seen in research clinics will be transferred to standard clinical pathways. The study will not prompt change in ongoing drug

treatment and study medication will not stop because the study has ended. Participants will be contacted and thanked for their participation. The end of the trial is defined as the last patient, last visit (LPLV) date.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Aripiprazole, sertraline, quetiapine

Primary outcome(s)
Improvement in depression measured using the Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR) weekly following randomisation

Key secondary outcome(s))
To compare the impact of the aripiprazole/sertraline combination versus quetiapine on the following secondary outcomes:
1. The trajectories of symptom change, measured via the QIDS-SR reported weekly from screening
2. Treatment satisfaction, measured via the Treatment Satisfaction Questionnaire for Medication (TSQM) at baseline and weeks 4, 14 and 24
3. Tolerability, measured via the Glasgow Antipsychotic Side-effect Scale (GASS) at baseline and weeks 4, 14 and 24
4. Pattern of medication adherence, measured via weekly questions in ePro regarding dosages of study medications taken on each of the preceding 7 days. This will be supported by the use of the Medication Adherence Rating Scale (MARS) at baseline and weeks 4, 14 and 24.
5. Pattern of non-randomised antidepressant/antipsychotic medication use, measured via analysis of concomitant medications weekly from screening
6. Change in anxiety symptoms, measured via the General Anxiety Disorder-7 (GAD-7) scale weekly from baseline
7. Change in manic symptoms and rates of relapse to a hypomanic or manic episode, measured via the Altman Self-Rating Mania Scale (ASRM) weekly from baseline
8. Psychosocial functioning, measured via the Work and Social Adjustment Scale (WSAS) at baseline and weeks 4, 14 and 24
9. Health-related quality of life, measured via the EQ-5D-5L questionnaire weekly from baseline
10. Capability well-being, measured via the ICEpop CAPability measure for Adults (ICECAP-A) and the Oxford CAPabilities Questionnaire-Mental Health (OxCAP-MH) at baseline and weeks 4, 14 and 24
11. Costs and incremental cost-effectiveness, based on the Health Economics Questionnaire (HEQ), measured at baseline and weeks 4, 14 and 24
12. Informal carers' health-related quality of life, capability well-being and costs of caring measured via the EQ-5D-5L, the ICEpop CAPability measure for Adults (ICECAP-A), the Oxford CAPabilities Questionnaire-Mental Health (OxCAP-MH) and the Caregiver Indirect and Informal Care Cost Assessment Questionnaire (CIIQ) at baseline and weeks 4, 14 and 24

Completion date
31/12/2027

Eligibility

Key inclusion criteria
Patients must fulfil all of the following criteria to progress to randomisation:
1. Aged 18 years old and over at the point of consent.
2. Able to provide written informed consent.
3. A current (i.e., within 7 days) Diagnostic and Statistical Manual-5-Text Revision (DSM-5-TR) confirmed diagnosis of a major depressive episode within bipolar disorder. This will be confirmed using the SCID-5-RV.
4. A current (i.e., within 7 days) QIDS-SR greater than 10.
5. Clinical uncertainty regarding the next course of treatment and judgement that the sertraline /aripiprazole combination and quetiapine treatment arms are both clinically appropriate and represent equipoise. This judgment includes consideration of reproductive risks.
6. In the opinion of the clinician, the participant is able to follow trial prescription instructions, complete weekly questionnaires and engage in weekly telephone calls with the cRAs throughout the 24-week follow-up period of the trial.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Any of the following criteria prevent progression to randomisation:
1. Currently participating in any other interventional clinical trial that may affect the outcome of ASCEnD.
2. DSM-5-TR defined severe substance use disorder.
3. Any known contraindications to aripiprazole, sertraline or quetiapine.
4. Currently pregnant, planning to become pregnant during the trial and/or breastfeeding.

Date of first enrolment
18/03/2024

Date of final enrolment

31/08/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust
St. Nicholas Hospital
Jubilee Road
Gosforth
Newcastle Upon Tyne
England
NE3 3XT

Study participating centre
Avon and Wiltshire Mental Health Partnership NHS Trust
Bath NHS House
Newbridge Hill
Bath
England
BA1 3QE

Study participating centre
Camden and Islington NHS Foundation Trust
St Pancras Hospital
4 St Pancras Way
London
England
NW1 0PE

Study participating centre
Oxford Health NHS Foundation Trust
Warneford Hospital
Warneford Lane
Headington
Oxford
England
OX3 7JX

Study participating centre
Birmingham and Solihull Mental Health NHS Foundation Trust
The Barberry
25 Vincent Dr
Birmingham
England
B1 3RB

Study participating centre
Cornwall Partnership NHS Foundation Trust
The Kernow Building
Wilson Way
Pool
Redruth
England
PL31 2QN

Study participating centre
Tees, Esk and Wear Valleys NHS Foundation Trust
Flatts Lane Centre
Flatts Lane
Normanby
Middlesborough
England
TS6 0SZ

Study participating centre
Hampshire and Isle of Wight Healthcare NHS Foundation Trust
Tatchbury Mount Hospital, Calmore
Southampton
England
SO40 2RZ

Study participating centre
Nottinghamshire Healthcare NHS Trust
D Floor
Institute of Mental Health
Triumph Road
Nottingham
England
NG7 2TU

Sponsor information

Organisation
Cumbria Northumberland Tyne and Wear NHS Foundation Trust

ROR
https://ror.org/01ajv0n48

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes