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Can taking amitriptyline tablets stop long-term pain from shingles?

Submission date
17/01/2022

Recruitment status
Recruiting

Registration date
27/01/2022

Overall study status
Ongoing

Last Edited
15/04/2025

Condition category
Infections and Infestations

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

Plain English Summary
Background and study aims
Shingles is a viral infection that causes a painful rash. This study aims to find out whether taking a low dose of amitriptyline soon after getting shingles can prevent the long-term pain associated with shingles

Who can participate?
Patients aged over 50 years who have been diagnosed by their GP with shingles.

What does the study involve?
Participants take tablets nightly for 10 weeks: half will be given low-dose amitriptyline and the other half will get placebo (dummy) tablets. Pain is assessed at 90 days after rash onset.

What are the possible benefits and risks of participating?
If starting amitriptyline early on does help, it is a cheap medicine that would prevent prolonged, difficult-to-treat pain for thousands of people. However, amitriptyline commonly causes side effects such as dizziness, dry mouth and constipation. It can also cause problems when used together with some other tablets. This study is needed so doctors can be sure that any benefits outweigh any harm.

Where is the study run from?
1. University of Bristol (UK)
2. Southampton University (UK)
3. Oxford University (UK)

When is the study starting and how long is it expected to run for?
July 2021 to July 2025

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
athena-study@bristol.ac.uk

Study website
https://athena-study.bristol.ac.uk/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2021-001101-78

IRAS number
1003967

ClinicalTrials.gov number

Nil known

Secondary identifying numbers
CPMS 50893, IRAS 1003967

Study information

Scientific Title
Amitriptyline for the prevention of post-herpetic neuralgia

Acronym
ATHENA

Study hypothesis
Prophylactic low-dose amitriptyline will reduce post-herpetic neuralgia in patients diagnosed with herpes zoster (shingles).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 18/10/2021, South West- Central Bristol Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, UK; +44 (0)207 104 8029, +44 (0)207 104 8068, +44 (0)207 104 8375; centralbristol.rec@hra.nhs.uk), REC ref: 21/SW/0130

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

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

Participant information sheet
https://athena-study.blogs.bristol.ac.uk/files/2022/01/ATHENA-PIL.pdf

Condition
Shingles

Interventions
Amitriptyline 10 mg tablets (or matched placebo tablet), increasing in 10 mg steps over 2 weeks as tolerated, to 30 mg maximum per day, for 70 days.

Total follow-up is 12 months, with participant surveys at baseline and 30, 60, 90, 120, 180 and 360 days after rash onset.

Randomisation:
Trial participants will be allocated in a 1:1 ratio to receive amitriptyline or placebo. Randomisation will be stratified by centre and minimised on age deciles, gender at birth, pain in the last 24 hours and shingles vaccination history. The randomisation sequence will be generated by the company Sealed Envelope™ using their online randomisation system, which will allocate the participant to a treatment arm. The person undertaking the randomisation and the participant will remain masked as to which treatment group this code refers.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Presence/absence of postherpetic neuralgia measured using a cut-off of ≥3/10 on numerical rating scale average pain in last 24 hours; Timepoint(s): 90 days after rash onset

Secondary outcome measures
1. The safety, tolerability and acceptability of amitriptyline assessed using patient-completed medication use, problems and hospitalisation sections of questionnaire at 30, 60 and 90 days, and by direct report by participant or clinician
2. Masking of participants assessed using the bang binding index in patient questionnaires at 30, 60 and 90 days post rash onset
3. Shorter and longer-term outcomes of pain, quality of life, mental well-being and frailty, assessed using the Zoster Brief Pain Inventory (ZBPI), 9-item patient health questionnaire (PHQ-9), 7-item general anxiety disorder questionnaire (GAD-7) and Tilburg Frailty Indicator, at 0, 90, 180 and 360 days post rash onset
4. The cost-effectiveness of low dose amitriptyline to placebo for the prevention of PHN using EQ-5D-5L and patient-completed healthcare resource use questions at 0, 90, 180 and 360 days post rash onset, and GP electronic medical records for the 12-month study period
5. Use of healthcare resources and analgesics assessed using patient-completed medication and healthcare resource use questions at 90, 180 and 360 days post rash onset, and GP electronic medical records for the 12-month study period

Overall study start date
01/07/2021

Overall study end date
31/07/2025

Eligibility

Participant inclusion criteria

1. Adults aged ≥50 years
2. Clinical diagnosis of herpes zoster (HZ)
3. Rash onset <144 hours

Participant type(s)
Patient

Age group
Adult

Lower age limit
50 Years

Sex
Both

Target number of participants
Planned Sample Size: 846; UK Sample Size: 846

Participant exclusion criteria
1. Inability to give informed consent
2. Third or more episode of herpes zoster
3. Known adverse reaction to amitriptyline or contraindications (monoamine oxidase inhibitors)
4. Current/recent (within previous two weeks) use of a tricyclic antidepressant
5. Prolonged QT interval or concomitant drugs that prolong the QT interval
6. Suicidal ideation
7. Heart block
8. Recent myocardial infarction (<4 weeks)
9. Immunosuppression
10. Significant bradycardia
11. Uncompensated heart failure
12. Hyperthyroidism
13. Severe liver disease
14. Phaeochromocytoma
15. Urinary retention
16. If female; current or planned (in next 3 months) pregnancy or breastfeeding
17. Currently (or recently, within the previous 4 months) enrolled in another CTIMP

Recruitment start date
30/03/2022

Recruitment end date
30/04/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Bristol
Senate House
Tyndall Avenue
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Study participating centre
University of Oxford
University Offices
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Study participating centre
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Sponsor type
University/education

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ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR129720

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal in approximately 2025. The researchers will publish a protocol in due course.

Intention to publish date
30/04/2027

Individual participant data (IPD) sharing plan
The final anonymised trial data set will be stored as restricted data on the data.bris research data repository for at least 5 years after the end of the study. Data will be made available after the end of the study to approved bona fide researchers only after their host institution has signed a data access agreement. Details of how to request access are available at the University of Bristol's data repository website.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Other publications	Qualitative interviews	31/07/2024	01/08/2024	Yes	No