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TOPPITS: Trial Of Proton Pump Inhibitors in Throat Symptoms

Submission date 17/04/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 17/04/2014	**Overall study status** Completed	
Last Edited 28/03/2022	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
This study aims to find out about the effect of proton pump inhibitor treatment on throat symptoms. We will be able to assess which specific throat symptoms respond, whether any patient characteristics can predict such a treatment response, how it impacts on quality of life, and find out how many dont respond to the treatment, for whom alternative approaches may be more appropriate.

Who can participate?
People aged over 18 having constant throat symptoms for more than 6 weeks can take part.

What does the study involve?
People joining the study take two tablets of the study medicine every day for 16 weeks, and come to the hospital clinic twice to see how the throat has responded. If you have not already been seen by one of the investigators, an appointment will be made for you at the special throat clinic within the next 4 weeks. Before this you may be given access to a DVD that explains more about the study at the specialist throat clinic. You will find out more information about the study and any questions you have will be answered. If you would like more time to consider taking part in the study, a second appointment can be arranged for you at a later date. If you are interested in taking part in the study you will be asked to sign a Consent Form to show your agreement and give your permission. A member of the research team will carry out a general health examination. They will measure and weigh you and they will take your medical history. You will then be asked to complete three questionnaires which should take about 5 to 10 minutes. These questionnaires ask about your throat symptoms. You will also need to have a photograph taken of your throat and voice box with a narrow endoscope after anaesthetic spray. You may have had a similar test similar cameras are used in all Ear Nose and Throat clinics. You will then be randomly allocated to receive either 16 weeks supply of lansoprazole or a placebo (dummy) treatment. An appointment will be made for you at the study clinic 4 months after your first visit. You will be seen by one of the research team and asked to repeat the three questionnaires. A final appointment will be made for you at the study clinic 8 months later. You will be asked to repeat the three questionnaires again. We have to do this three times to be able to measure any change in your scores.

What are the possible benefits and risks of participating?
We cannot promise the study will help you directly but the information we get from this study will help improve the treatment of people with persistent throat symptoms. We want you to be safe in this study at all times, but all medical treatments carry some risk. Lansoprazole is a very safe drug which is used in thousands of NHS patients with stomach problems every month. However, if you react badly to the drug your doctor will be able to change your medication and treat you immediately. If the doctor needs to find out which treatment you are taking, this information is available 24 hours a day, seven days a week.

Where is the study run from?
The study will run at three initial sites in the UK (Newcastle upon Tyne, Sunderland and Nottingham), in the first 6 months. A further three sites (Brighton, Glasgow and Manchester) will join after this period, and the study will run for a further 18 months at six sites.

When is the study starting and how long is it expected to run for?
April 2014 to October 2017

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

Who is the main contact?
Miss Gillian Watson
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2013-004249-17

Protocol serial number
16317

Study information

Scientific Title
A randomised, placebo-controlled trial of extra-oesophageal reflux treatment in the management of upper respiratory symptoms

Acronym
TOPPITS

Study objectives
Is treatment with lansoprazole for four months (16 weeks) effective in patients with persistent throat symptoms, versus placebo?

Ethics approval required
Old ethics approval format

Ethics approval(s)
13/NE/0336; First MREC approval date 02/12/2013

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Ear, nose and throat; Subtopic: Ear (all Subtopics); Disease: Ear, nose & throat

Interventions
Treatment with either 30 mg (twice daily) dose of the proton pump inhibitor lansoprazole or placebo on a 1:1 basis for 16 weeks; Follow Up Length: 12 month(s); Study Entry : Single Randomisation only

A blocked allocation (permuted random blocks of variable length) system will be used to allocate patients in a 1:1 ratio stratified by centre and baseline severity (two groups, on the basis of the Reflux Symptom Index score). Block size will not be disclosed to the investigators and the computer-generated allocation list will be produced by an individual not otherwise involved with the study in order to ensure concealment of allocation. Randomisation will be administered centrally via Newcastle Clinical Trials Unit using a secure web based system. The PI or delegated personnel named on the delegation log will obtain the randomisation number via this system (http://apps.ncl.ac.uk?random/ - available 24 hours a day).

Details of a nominated CTU contact for randomisation will be notified to sites.
Randomisation will generate a treatment number for each participant that links to the corresponding allocated study drug (blinded), in accordance with block size and strata. The treatment number must be clearly documented by the investigator on the trial prescription to ensure the study pharmacist dispenses the correct study medication.

Intervention Type

Drug

Phase
Not Applicable

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

Primary outcome(s)
Symptomatic response measured using the Total Reflux Symptom Index (RSI) at 16 weeks/4 months in the treatment and placebo groups

Key secondary outcome(s))
1. Adverse events measured using standard reporting procedures, as recommended by Good Medical Practice, throughout the 12 month study period
2. Compliance with intervention, as measured by reported medication taken and return of unused tablets at the 16-week primary outcome measure timepoint
3. Longer-term symptomatic response measured using the Reflux Symptom Index (RSI) at 12 months from randomisation
4. Symptomatic response, omitting the reflux symptoms, measured using the total laryngopharyngeal item RSI score omitting the GORD item (RSI-HB, score 0 to 40) at 16 weeks and 12 months
5. Symptoms measured using the 34-item Comprehensive Reflux Symptom Score and the 43-item Laryngopharyngeal Health-Related Quality of Life (LPR HRQL) at 16 weeks and 12 months
6. Utility of baseline laryngeal mucosal changes recorded by the Reflux Finding Score (RFS) at randomisation
7. Patient prediction of allocated intervention measured using direct questioning at 16 weeks
8. Patient-reported satisfaction with the trial measured using a five-point scale at 12 months

Completion date
01/10/2017

Eligibility

Key inclusion criteria
1. Referred with a persistent (over six weeks) primary throat symptom - globus, hoarseness, throat clearing, throat discomfort, choking spasms, excess mucus/postnasal drip.
2. Informed consent to participate in entry screen.
3. Score over 10 on the non-heartburn items of the Respiratory Symptoms Index.
4. Patient has provided written informed consent for participation in the study prior to any study-specific procedures after reading the appropriate information and the required cooling off period has ensued
Target Gender: Male & Female ; Lower Age Limit 18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
346

Key exclusion criteria
1. Those with an RSI score excluding the lower GI item of <10.
2. Patients who are not willing to undergo flexible endoscopy could not by definition be included.
3. Inability to complete the relevant questionnaires.
4. Patients under 18 years old.
5. Endoscopic evidence of specific laryngopharyngeal pathology that would ordinarily be treated by surgical intervention or be investigated by specific investigations. This would include suspected neoplasia/dysplasia, prominent Reinke's oedema or unilateral vocal fold polyp, vocal cord palsy and rarities such as amyloid, Wegener's, sarcoid.
6. Confirmed or likely, current or prior malignancy of head and neck or oesophagus.
7. Performing voice user.
8. Pregnant or lactating woman. Woman of child bearing potential must be using adequate contraception.
9. Currently on acid suppressant, acid neutralisers and alginates and unwilling to discontinue for 4 weeks pre study washout period.
10. Prior adverse reaction to proton pump inhibitor.
11. Severe hepatic dysfunction.
12. Patients taking clopidogrel or Warfarin.
13. Patients taking Phenytoin.
14. Patients taking systemic antifungal treatment (specifically itraconazole, ketoconazole, posaconazole and voriconazole).
15. HIV positive/Patients taking Antiviral medications (atazanavir, nelfinavir, raltegravir, saquinavir, tipranavir).
16. Patients taking digoxin, cyclosporine, methotrexate, erlotinib, lapatinib, tacrolimus, sucralfate, escitalopram, fluvoxamine, St Johns wort, clozapine, Ulipristal or Cilostazol.
17. Previous participation in this study.
18. Use of other investigational study drugs within 30 days prior to study entry.

Date of first enrolment
27/05/2014

Date of final enrolment
01/10/2017

Locations

Countries of recruitment

United Kingdom

England

Study participating centre
Newcastle University
Newcastle Upon Tyne
United Kingdom
NE2 4HH

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme; Grant Codes: 12/01/04

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

The anonymised data will be available, in line with the Newcastle University Research Data Service. The data will be entered into data.ncl for researchers to access

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/01/2021	26/01/2021	Yes	No
Results article	Cross-sectional study	01/03/2022	28/03/2022	Yes	No
Protocol article	protocol	01/04/2016		Yes	No
Basic results			28/05/2020	No	No
HRA research summary			28/06/2023	No	No
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