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Treat to target in gout

Submission date	Recruitment status	[X] Prospectively registered
17/04/2019	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
12/06/2019	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
08/04/2025	Musculoskeletal Diseases	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Gout is a common arthritis that affects one in forty people in the UK. It results from a high level of uric acid in the body which forms urate crystals inside the joints. From time to time, these crystals shake loose from their deposit and cause severe joint pain and swelling. These flares usually last for one to two weeks. Flares are treated with anti-inflammatory tablets such as ibuprofen. However, anti-inflammatory tablets do not dissolve the urate crystals. Other tablets such as allopurinol can lower the uric acid level to below a target level, and slowly dissolve the crystals. These are safe treatments that have been used for many years. However, whether their use reduces the number of gout flares is unknown. The aims of this study are to find out if long-term use of tablets such as allopurinol reduces the number of gout flares and improves well-being and to also find out if this treatment is cost-effective for the NHS.

Who can participate?
Patients aged 18 years and over with gout who have had a flare of gout in the previous 12 months

What does the study involve?
Participants are randomly allocated to receive one of the following two treatments: allopurinol with the dose gradually increased aimed at reducing blood uric acid to below target level, or usual gout care from their GP including the option to start allopurinol depending on symptoms. People in the first group need treatment visits with a practice nurse in order to adjust the dose of allopurinol to reduce uric acid level sufficiently to allow the urate crystals to dissolve. In addition to the visits to increase the dose of allopurinol, there are three other visits for people taking part in the study. These visits occur at study start, and yearly for 2 years. Information on health, wellbeing and medication use are collected, and blood pressure, height, weight, kidney function and uric acid level are measured at the visits. People taking part in the study are asked to record details of each gout flare they experience while in the study. The main outcome of the study is the number and severity of gout flares. This and the other information collected are compared between the groups. The cost of treatment and overall wellbeing are used to find out if this treatment is cost-effective for the NHS. After the 2-year study ends, participants are asked to continue to provide information about gout flares for a further 2 years. Information about other illnesses, hospital admissions and medications prescribed are collected from their GP. The information collected is compared between the groups.

What are the possible benefits and risks of participating?
Any medications that will be advised to be used for gout in this study will be currently available treatments that will be prescribed in line with guidelines. As with any medication, the treatments for gout can sometimes cause side effects but it is rare to suffer any serious upset. The researchers currently do not know the benefit to patients taking part in the study. However, this study will help them to learn more about how gout should be treated and improve the care of patients with gout in the future.

Where is the study run from?
The study is being run from the University of Nottingham and the Keele Clinical Trials Unit is managing the study. The study is recruiting patients in East Midlands, West Midlands and Wessex (UK)

When is the study starting and how long is it expected to run for?
The study plans to start recruitment in summer 2019 and patients will be in the study for 2 years with an additional 2-year long-term follow-up.

Who is funding the study?
National Institute of Health Research (NIHR) Health Technology Assessment (HTA) programme (UK)

Who is the main contact?
Steff Garvin
s.garvin@keele.ac.uk

Study website
https://www.keele.ac.uk/t2t

Contact information

Type(s)
Scientific

Contact name
Dr Abhishek Abhishek

Contact details
Nottingham City Hospital
Nottingham
United Kingdom
NG51PB
+44 (0)1782 732950
abhishek.abhishek@nottingham.ac.uk

Type(s)
Public

Contact name
Miss Steff Garvin

Contact details

Keele University
Staffordshire
United Kingdom
ST5 5BG
+44 (0)1782 732950
s.garvin@keele.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
263669

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
19023; HTA 17/82/02, IRAS 263669

Study information

Scientific Title
What is the clinical and cost effectiveness of using a goal-directed allopurinol-based treat-to-target protocol in people with recurrent gout flares?

Acronym
T2T

Study objectives
To evaluate the effectiveness of allopurinol-based treat-to-target ULT versus usual general practitioner (GP) care on number of gout flares over 2 years.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 10/06/2019, North West - Liverpool East Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, United Kingdom; +44 (0)207 104 8345, +44 (0) 207 104 8019; nrescommittee.northwest-liverpooleast@nhs.net), ref: 19/NW/0310

Study design
Parallel-arm multicentre randomized controlled trial with 1-year internal pilot and 2-year long-term extension phase

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Gout

Interventions
Participants will be randomised to one of two interventions. Randomisation: 1:1 individual randomisation stratified by region and prior intolerance to Colchicine.

Intervention arm 1: Allopurinol-based treat-to-target Urate Lowering Treatment (ULT) (delivered by practice nurses in primary care). Patients will have commence on a dose of 100 mg of allopurinol or have this increased by 100 mg if already on treatment. Treatment will follow 'a treatment-to-target' approach, i.e. patients will be prescribed low-dose ULT initially, and the dose increased monthly, guided by blood-test results, until the urate level is sufficiently below the saturation point (i.e. less than 360 µmol/L). Other ULTs will be prescribed if allopurinol is not tolerated.

Intervention arm 2: Usual GP care: Patients will be advised to consult their GP as usual and receive treatment for gout flares and urate lowering treatment according to GP's usual practice.

Each participant in the study for 4 years, 2 years each in the RCT and long-term extension respectively.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Number of gout flares in the first 2 years measured by patient initiated SMS service or acute gout flare diary

Secondary outcome measures
1. Number of gout flares in months 1-12, measured by self-report using SMS or gout flare diary
2. Number of gout flares in months 13-24, measured by self-report using SMS or gout flare diary
3. Tophus count, measured by visual inspection at baseline, year 1 and year 2
4. Size of largest tophus, measured using vernier calipers at baseline, year 1 and year 2

5. Daily pain score measured by self-report using SMS or gout flare diary during gout flare
6. Quality of life measured by EQ-5D-5L during gout flares
7. GIS after flare resolution, measured by completing a questionnaire at baseline, year 1 and year 2 and during gout flares
8. Serum urate: proportion hitting the target serum urate level (<360 µmol/L) and continuous variable at year 1 and 2, measured from a blood sample taken at baseline and year 1 and year 2 post randomisation research visits
9. Quality of life measured by EQ-5D-5L between gout flares at baseline, year 1 and year 2
10. ULT (name and dose) measured by self-report during treatment visits and at year 1 and year 2
11. Treatment satisfaction measured by TSQM-II at year 1 and year 2 post randomisation
12. Returned pill count documented on a CRF at research year 1 and year 2 post randomisation visits
13. Compliance with ULT measured by MMAS-8 scale at year 1 and year 2
14. Serum creatinine and estimated GFR measured from a blood test at screening, year 1 and year 2 and during treatment visits in the intervention arm
15. Urine albumin-creatinine ratio measured from a urine sample at baseline, year 1 and year 2
16. Primary-care consultations for gout, measured by self-report and general practice record search at year 4
17. Hospitalizations due to gout, measured by self-report and general practice record search at year 4
18. Other prescriptions for treating flares of gout, measured by general practice record search at year 4
19. Investigations for gout, measured by general practice record search at year 4
20. Incident cardiovascular diseases, hypertension, diabetes, measured by general practice record search at year 4
21. Incidence or progression of CKD, measured by: general practice record search at year 4
22. Death, measured by general practice record search at year 4
23. Adverse events (AE), measured by self-report at 2 years
24. Cost-effectiveness, measured by health economic analysis of all data at 2 years

Overall study start date
01/01/2019

Completion date
31/08/2028

Eligibility

Key inclusion criteria
1. Age ≥18 years
2. Ability to give informed consent
3. Meets the clinical American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for gout
4. ≥1 flare of gout in the previous 12 months
5. Serum urate ≥360 µmol/L regardless of current ULT

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
466

Total final enrolment
468

Key exclusion criteria
1. Previous allopurinol side-effects that contraindicate its prescription
2. Dementia, severe enduring mental illness i.e. mental health illness that makes receiving the study information and initial screening questionnaire from GP a stressful experience
3. Unable to comply with study procedures
4. Life expectancy less than 12 months
5. Cancer treatment, i.e. surgery, radiotherapy, or chemotherapy in the previous 12 months
6. Solid organ transplant
7. Cirrhosis
8. Autoimmune rheumatic disease i.e. rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, connective tissue diseases, vasculitis, giant cell arteritis, polymyalgia rheumatica, inflammatory arthritis associated with inflammatory bowel disease, reactive arthritis, ankylosing spondylitis
9. Inflammatory bowel disease
10. Current long-term daily oral corticosteroid treatment defined as continuous use for ≥30 days or current immunosuppressive treatments
11. Stage 4/5 CKD i.e. eGFR < 30 ml/min
12. Pregnant, breastfeeding or planning to become pregnant in the next 4 years

Date of first enrolment
30/06/2019

Date of final enrolment
02/05/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
East Midland Clinical Research Network
Level 1 Knighton Street Outpatients
Leicester Royal Infirmary

Leicester
United Kingdom
LE1 5WW

Study participating centre
West Midland Clinical Research Network
Unit 9 Greyfriars Business Park
Greyfriars Road
Frank Foley Way
Stafford,
United Kingdom
ST16 2ST

Study participating centre
Wessex Clinical Research Network
Unit 7, Berrywood Business Village
Tollbar Way
Hedge End
Southampton
United Kingdom
SO30 2UN

Study participating centre
London CRNs (Noclar, North London, South London, and Lutton Essex and Herts)
1st Floor, Bloomsbury Building
St Pancras Hospital
4 St Pancras Way
London
United Kingdom
NW1 0PE

Study participating centre
Yorkshire and Humber CRN
Oak House
Moorhead Way
Bramley
Rotherham
United Kingdom
S66 1YY

Study participating centre

Thames Valley and South Midlands CRN
Unipart House
NIHR CRN: Thames Valley And South Midlands Offices Level 2 West
Garsington Rd
Cowley
Oxford
United Kingdom
OX4 2PG

Sponsor information

Organisation
University of Nottingham

Sponsor details
East Atrium Jubilee Conference Centre
Jubilee Campus
Nottingham
England
United Kingdom
NG81DH
+44 (0)1158467906
sponsor@nottingham.ac.uk

Sponsor type
University/education

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The protocol will be available on the NIHR HTA journals library but has yet to be published. The results of this study will be shared at medical conferences and through publication in academic journals.

Intention to publish date
31/08/2028

Individual participant data (IPD) sharing plan
The datasets generated and analysed during the current study will be available upon request from the Chief Investigator. Requests should be emailed to the sponsor using the sponsor contact details, in which an external data request process will be initiated and considered. Consent from participants will be obtained for use of anonymous data in future research and will be available for 7 years after the study has ended.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No