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Omega–3 fatty acids for preventing acute attacks of gout - a feasibility study

Submission date
04/03/2018

Recruitment status
No longer recruiting

Registration date
08/08/2019

Overall study status
Completed

Last Edited
22/11/2022

Condition category
Musculoskeletal Diseases

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Background and study aims
Omega-3 fatty acids block several pathways through which urate crystals that cause gout induce inflammation. Early findings demonstrate that low levels of omega-3 fatty acids in the blood are associated with frequent gout attacks, also called flares. The aim of this study is to examine the feasibility of conducting a larger trial to definitely find out whether omega-3 fatty acids prevent flares of gout when starting urate-lowering treatment (ULT).

Who can participate?
Patients aged over 18 with gout who have experienced a gout attack in the previous 12 months

What does the study involve?
Participation in the study involves three research visits, and about four treatment visits over a 28-week period, with an initial blood test. If the participants' uric acid level is high enough, they can continue into the study and are invited for a baseline visit. The participant is randomly allocated to have either omega-3 fatty acid or matching placebo (dummy) capsules filled with olive oil. They are also given urate-lowering treatment (either allopurinol, febuxostat, or benzbromarone) to be started 4 weeks later. At week 7 of the treatment, participants come for an up-titration follow-up visit. The participants are in the study for 28 weeks. The participant also completes a questionnaire at the first and last visits. If the participant experiences any gout attacks during the study period, they are asked to fill out a gout diary.

What are the possible benefits and risks of participating?
All participants in this study will receive urate-lowering treatment. Research has shown that just under 40% of people with gout who meet the eligibility criteria to start potentially curative long term urate-lowering treatment are started on it by their GP in the UK. Thus, participants can expect to be cured of gout if they participate in this study. Omega-3 fatty acids can cause transient intolerance and side-effects. They do not carry any risk of serious long-term side effects. Should this happen, the participant would be eligible to continue in the study without taking the study drugs or reduce the dose if this is acceptable to them. Similarly, urate-lowering treatments do not carry any risk of serious long-term side effects. If someone develops an intolerance to one of the urate-lowering treatments, they will be started on an alternative urate-lowering drug. The start and end of study research visits will last between one and one and a

half hours. The other visits are relatively short and will last between 15 to 30 minutes. These additional visits to check serum uric acid and increase the dose of allopurinol are standard of care. The visits were felt to be acceptable at a PPI meeting.

Where is the study run from?
University of Nottingham, City Hospital (UK)

When is the study starting and how long is it expected to run for?
February 2019 to August 2020 (updated 16/10/2020, previously: March 2020)

Who is funding the study?
Versus Arthritis UK

Who is the main contact?
Dr Abhishek Abhishek

Contact information

Type(s)
Scientific

Contact name
Dr Abhishek Abhishek

Contact details
Division of Academic Rheumatology
The University of Nottingham
Room A27
Clinical Sciences Building
City Hospital
Nottingham
United Kingdom
NG5 1PB

Type(s)
Scientific

Contact name
Dr Amy Fuller

Contact details
Academic Rheumatology
The University of Nottingham
Room A23
Clinical Sciences Building
City Hospital
Nottingham
United Kingdom
NG5 1PB
+44 (0)115 8231761
amy.fuller@nottingham.ac.uk

Additional identifiers

EudraCT/CTIS number
2018-000963-99

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS: 39988

Study information

Scientific Title
Omega–3 fatty acids for the prophylaxis of acute attacks of gout on initiating urate-lowering treatment – a feasibility study for a randomised controlled trial

Acronym
SOGAS

Study objectives
It is hypothesized that omega-3 fatty acids will prevent acute attacks of gout in patients commenced on urate-lowering treatment. The overall aim of this feasibility study is to establish the metrics for conducting a multicentre randomised controlled trial to definitively test whether omega-3 fatty acids can prevent acute attacks of gout in patients starting on urate-lowering treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/12/2018, East Midlands – Derby Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, Nottinghamshire, NG1 6FS, UK; Tel: +44 (0)207 104 8109/+44 (0) 207 104 8237; Email: nrescommittee.eastmidlands-derby@nhs.net), REC ref: 18/EN/0324

Study design
Feasibility randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

Participant information sheet

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

Interventions
Randomisation: 1:1 individual randomisation

Randomisation time: Randomisation will occur once the results of screening blood tests performed at the screening visit are reviewed and eligibility and ongoing consent are confirmed. Patients will be randomized into two arms using randomly permuted block sizes. Stratification or minimization will not be used.

Intervention: omega-3 fatty acid capsules (4 g/day; containing 3.36 g of omega-3 fatty acids)
Control: placebo capsules (4 g olive oil/day)

After four weeks participants in both arms will be commenced on up-titrated urate-lowering treatment as recommended by the British Society for Rheumatology Guidelines. The participants will be randomised and given the IMP or matching placebo for 14 weeks. The participants will also be given a supply of urate-lowering treatment (typically allopurinol 100 mg/day or febuxostat 80 mg/day if allopurinol is contraindicated or has previously caused side-effects) to be started 4 weeks later and a rescue pack of oral prednisolone tablets at a dose of 30 mg/day for 1 week to be taken during an acute gout attack. In case prednisolone is contraindicated, the rescue pack will contain Naproxen 500 mg twice a day for 1 week with omeprazole 20 mg/day. The participants will be specifically asked not to start urate-lowering treatment until day 28. They will be contacted by phone, or text 2-3 days prior to day 28 as a reminder.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Omega-3 fatty acids

Primary outcome measure
Dropout rate defined as number of patients randomised that remain in the study until end of follow-up at 28 weeks

Secondary outcome measures
1. Recruitment rate recorded as the number of eligible participants based on self-reported number of gout flares in initial gout questionnaire who are randomised in the study.
2. The proportion of patients approached by the GP with information about the study and requested to return the reply slip to the study team, who complete the following by the end of the 28-week study:
2.1. Reply to Academic Rheumatology, University of Nottingham
2.2. Meet the eligibility criteria on telephone screening and based on reply to the initial gout

questionnaire
2.3. Agree for screening visit
2.4. Meet the eligibility criteria after checking serum uric acid, full blood count, liver and kidney function tests
2.5. Are randomised into the trial
3. The number of gout flares measured using gout diary between weeks 5 and 28 of the study
4. The severity of gout flares defined as an average of daily pain visual analogue scale (0-100) during a gout flare between weeks 5 and 28 of the study. Calculated by sum of daily pain scores divided by number of days on which the gout flare is present
5. The number of days gout flares were experienced by each participant measured using gout diary between weeks 5 and 28 of the study
6. The number of participants who withdrew themselves from the study due to side effects related to omega-3 fatty acids between weeks 0 and 28 of the study
7. The number of participants not on ULT at each GP surgery at the start of recruitment when surgeries complete the mail-out
8. Compliance with study drug measured by capsule count at weeks 14 and 28

Overall study start date
05/02/2019

Completion date
27/07/2020

Eligibility

Key inclusion criteria
1. GP/physician-diagnosed gout
2. Meets the American College of Rheumatology/European League against Rheumatism (EULAR) classification criteria for gout
3. Willing to commence on urate-lowering treatment
4. Serum uric acid ≥ 360 µmol/L at the screening visit
5. Age ≥ 21 years at the screening visit
6. Able to give informed consent
7. No change in the average weekly dose of analgesics for at least 4 weeks prior to the screening visit
8. Be able to adhere to the study visit schedule and other protocol requirements
9. Subjects able to communicate well with the investigator or designee, to understand and comply with the requirements of the study and to understand and sign the written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
60

Total final enrolment
60

Key exclusion criteria
1. Other defined inflammatory arthritis e.g. reactive arthritis, rheumatoid arthritis, psoriatic arthritis, seronegative spondyloarthropathy, Lyme's disease, or plaque psoriasis
2. Other autoimmune inflammatory conditions like moderate/severe asthma or inflammatory bowel disease requiring corticosteroids or immune-suppressing treatments
3. Active solid organ cancer
4. Dementia
5. Serious co-morbidities preventing prescription of treatment
6. On regular daily NSAIDs, prednisolone, and unable to discontinue them
7. On long-term anticoagulation: Because of the mild increase in bleeding time with 4 gm/day omega-3 fatty acids, there is a potential interaction with warfarin and an increased possibility of haemorrhage in patients at high risk because of severe trauma, surgery, etc. Patients receiving anticoagulant therapy will therefore be excluded.
8. Oral, intramuscular, intra-arterial, or intravenous corticosteroids during the last 1 month
9. Known allergy to omega-3 fatty acids, gelatine, olive oil, and soya
10. Pregnant or planning to become pregnant during the treatment period
11. Use of any investigational (unlicensed) drug within 3 month prior to screening or within 5 half-lives of the investigational agent, whichever is longer
12. Evidence of serious uncontrolled concomitant medical condition, including cardiovascular, nervous system, pulmonary, renal, hepatic, endocrine, gastro-intestinal disease or epilepsy, which in the opinion of the investigator makes them unsuitable for the study
13. Significant haematological or biochemical abnormality:
13.1. Haemoglobin <85 g/L
13.2. WCC <3.5 x 109/L
13.3. Neutrophils <1.5 x 109/L
13.4. Platelets <100 x 109/L
13.5. ALT >1.5 times upper limit of normal
13.6. Creatinine >2 times upper limit of normal

Potential participants deemed ineligible at the screening will be allowed a second screening visit if the ineligibility status is temporary e.g. recent corticosteroid use

Date of first enrolment
27/03/2019

Date of final enrolment
30/03/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Nottingham
Academic Rheumatology
Clinical Sciences Building
City Hospital Nottingham
Nottingham
United Kingdom
NG5 1PB

Sponsor information

Organisation
Nottingham University Hospital NHS Trust

Sponsor details
Research and Innovation
Queens Medical Center
Nottingham
England
United Kingdom
NG7 2UH
+44 (0)115 9249924 ext 70659
researchsponsor@nuh.nhs.uk

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05y3qh794

Funder(s)

Funder type
Charity

Funder Name
Arthritis Research UK

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The results of this study will be published in peer-reviewed medical journals.

Intention to publish date
01/03/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Abhishek Abhishek (abhishek.abhishek@nottingham.ac.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version V3.0	23/05/2019	09/08/2019	No	No
Protocol file	version V5.2	01/04/2020	29/09/2020	No	No
Basic results		16/08/2021	03/09/2021	No	No
Results article		25/10/2022	22/11/2022	Yes	No