ISRCTN16717773 https://doi.org/10.1186/ISRCTN16717773

A proof of concept study to test whether talarozole has an effect on hand osteoarthritis in the base of thumb joint

Submission date
10/02/2022

Recruitment status
Recruiting

Registration date
16/02/2022

Overall study status
Ongoing

Last Edited
23/01/2026

Condition category
Musculoskeletal Diseases

[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
The base of thumb joint can commonly be affected by osteoarthritis (OA). This can lead to pain, stiffness, swelling, and difficulty performing activities such as writing, opening jars, or turning keys. Treatment options may include advice on lifestyle factors that may contribute, hand exercises, pain relief such as anti-inflammatory gels or paracetamol, splints, and steroid injections. A surgical procedure called a trapeziectomy (removal of the trapezium bone at the base of the thumb) may be performed where there is ongoing pain and/or severe disability after trying other more conservative treatments. There are currently no drugs that can slow the progression of OA.
Recent genetic studies have shown that some individuals with severe hand OA have variation in a gene named ALDH1A2. This gene is responsible for making retinoic acid, which is a natural anti-inflammatory agent. Researchers at the University of Oxford have shown that retinoic acid levels rapidly decrease after cartilage injury, a primary cause of OA. A group of drugs known as Retinoic Acid Metabolism Blocking Agents (RAMBAs) may help to prevent this decrease in retinoic acid, and have an anti-inflammatory effect in patients with base of thumb OA. If this drug is proven to be effective it could provide a new treatment option, reducing pain, progression, and the need for surgery

Who can participate?
Men or women aged 18-79 years who have been scheduled for trapeziectomy surgery for base of thumb osteoarthritis at a participating study site.

What does the study involve?
• There are two study visits at the participating hospital site plus two telephone appointments over a period of 4-16 weeks.
• Visit 1 Screening: Consent process and collection of information for eligibility assessment.
• Visit 2 Baseline telephone call: allocation by computer to study medication and collection from pharmacy (talarozole or placebo).
• Visit 3 Day of Surgery: removal of fluid from thumb joint and collection of bone and cartilage normally washed out/discarded during surgery.

• Visit 4 Post-surgery telephone follow-up: health and medication review.
• Participants will be prescribed study medication (talarozole or placebo) at Visit 2 (Baseline) and asked to take the study medication daily for approximately 14 days leading up to their trapeziectomy surgery. The exact timing may vary depending on the date of surgery with a maximum of 21 days on the study medication.
• A grip strength and key pinch test will be carried out at Visit 1 (Screening) to assess level of hand function and strength.
• Blood tests will be taken at Visit 1 (Screening) and Visit 3 (Day of Surgery).
• Participants will be asked to score the severity of their hand pain daily for up to 4 weeks prior to their surgery.
• Questionnaires: completion of 2 online/postal questionnaires on hand health, hand function and overall health at Visits 2 (Baseline) and 3 (Day of Surgery) and one online/postal questionnaire about overall study experience at Visit 4 (Post-surgery follow-up).

What are the possible benefits and risks of participating?
There is no direct benefit to the participant from taking part in this study. The short duration of medication in this study is to allow testing of whether the drug has the expected effect in the joint and is not expected to cause a substantial change to the participant's osteoarthritis or need for hand surgery. The study will generate useful information which may benefit others in the future and help the development of new treatments for osteoarthritis. During the study participants will be monitored closely by a doctor and this monitoring may have indirect health benefits. Possible risks form taking part include:
When taking blood samples, minor bruising at the needle puncture site may occur in some people.
When taking any form of medication people can sometimes experience unwanted side effects. Talarozole has been tested in more than 200 people taking part in other clinical trials. From this information, talarozole is generally well tolerated but may cause some side effects. Participants will be monitored for any possible side effects of the study medication during the study.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
October 2020 to June 2026

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Mandy Lewis, Ramboh-1@kennedy.ox.ac.uk

Contact information

Type(s)
Scientific

Contact name
Ms Mandy Lewis

Contact details

Kennedy Institute of Rheumatology
NDORMS
University of Oxford
Roosevelt Drive
Oxford
United Kingdom
OX3 7F7
+44 1865 612643
Ramboh-1@kennedy.ox.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
291242

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 50535, MR/S035664/1

Study information

Scientific Title
Retinoic acid metabolism blocking agents (RAMBAs) to treat osteoarthritis of the hand: A 2-arm double-blind randomised controlled proof of concept study

Acronym
RAMBOH-1

Study objectives
Current study hypothesis as of 05/01/2024:
The study will test the hypothesis that the retinoic acid metabolism blocking agent talarozole, will increase all-trans retinoic acid responsive gene expression and reduce inflammatory gene regulation in the articular cartilage of trapezia of individuals with symptomatic thumb carpometacarpal joint osteoarthritis compared to placebo.

Previous study hypothesis:
The study will test the hypothesis that the retinoic acid metabolism blocking agent, talarozole, will increase all-trans retinoic acid responsive gene expression in the articular cartilage of trapezia of individuals with symptomatic thumb carpometacarpal joint osteoarthritis compared to placebo.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 05/10/2021, East Midlands - Nottingham 2 Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 (0)207 104 8009; nottingham2.rec@hra.nhs.uk), ref: 21/EM/0220

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Osteoarthritis of the hand

Interventions
Current intervention as of 26/08/2025:
RAMBOH-1 is a two-arm double-blind randomised controlled proof of concept study using a pharmacological intervention. The study will take place in selected UK NHS hospitals, which will perform all study activities from recruitment to provision of intervention and follow-up.

Participants are randomised 1:1 to either talarozole or placebo. The dosing regimen is two capsules (2 x 1 mg capsules of talarozole / 2 placebo capsules) are to be taken orally, once a day in the morning for 14 days prior to surgery (with day of surgery being day 14).

There are two study visits plus two telephone appointments over a period of 4-16 weeks. Prior to enrolment in the study there will be a Pre-screening telephone call in order to assess key eligibility criteria.
Participants will be assessed at the following time points:
Visit 1. Screening (-70 to -1 days)
Visit 2. Baseline (telephone appointment) (Day 0): Randomisation
Visit 3. Day of Surgery (Day 10 - Day 21)
Visit 4. Post-surgery follow-up (telephone appointment*) (Day of Surgery + 7-21 days)

A computerised randomised system will be used for allocation of participants, to ensure equipoise.

Timeline for the study
Recruitment will be active for 18 months followed by a 4-week follow-up period until the final participant’s study follow-up appointment.

Participant experience
There are two study visits plus two telephone appointments over a period of 4-16 weeks. Visits will take place at the participating hospital site. Two of the four appointments are routine NHS hospital visits with additional study procedures.
Blood tests will be taken at Visit 1 (Screening) and Visit 3 (Day of Surgery). At Visit 1 there will be a hand examination including measures of hand function. Questionnaires will be completed at

Visit 2 (Baseline), Visit 3 (Day of Surgery), and Visit 4 (Post-surgery follow-up).
Participants will be asked to score the severity of their hand pain daily for up to 4 weeks prior to their trapeziectomy.

_____

Previous interventions as of 23/07/2024:

RAMBOH-1 is a 2-arm double-blind randomised controlled proof of concept study using a pharmacological intervention. The study will take place in selected UK NHS hospitals, which will perform all study activities from recruitment to provision of intervention and follow-up.

Participants are randomised 1:1 to either talarozole or placebo. The dosing regimen is 2 capsules (2 x 1mg capsules of talarozole / 2 placebo capsules) are to be taken orally, once a day in the morning for 14 days prior to surgery (with day of surgery being day 14).

There are two study visits plus two telephone appointments over a period of 4-16 weeks. Prior to enrolment in the study there will be a Pre-screening telephone call in order to assess key eligibility criteria.
Participants will be assessed at the following time points:
Visit 1. Screening (-70 to -7 days)
Visit 2. Baseline (telephone appointment) (Day 0): Randomisation
Visit 3. Day of Surgery (Day 10 - Day 21)
Visit 4. Post-surgery follow-up (telephone appointment*) (Day of Surgery + 7-21 days)
*A face to face visit for follow-up pregnancy testing will be required for women of child bearing potential

A computerised randomised system will be used for allocation of participants, to ensure equipoise.

Timeline for the study
Recruitment will be active for 18 months followed by a 4 week follow-up period until the final participant’s study follow-up appointment.

Participant experience
There are two study visits plus two telephone appointments over a period of 4-16 weeks. Visits will take place at the participating hospital site. Two of the four appointments are routine NHS hospital visits with additional study procedures.
Blood tests will be taken at Visit 1 (Screening) and Visit 3 (Day of Surgery). At Visit 1 there will be a hand examination including measures of hand function. Questionnaires will be completed at Visit 2 (Baseline), Visit 3 (Day of Surgery), and Visit 4 (Post-surgery follow-up).
Participants will be asked to score the severity of their hand pain daily for up to 4 weeks prior to their trapeziectomy.

_____

Previous interventions as of 05/01/2024 to 23/07/2024:

RAMBOH-1 is a 2-arm double-blind randomised controlled proof of concept study using a pharmacological intervention. The study will take place in selected UK NHS hospitals, which will perform all study activities from recruitment to provision of intervention and follow-up.

Participants are randomised 1:1 to either talarozole or placebo. The dosing regimen is 2 capsules (2 x 1mg capsules of talarozole / 2 placebo capsules) are to be taken orally, once a day in the morning for 14 days prior to surgery (with day of surgery being day 14).

There are two study visits plus two telephone appointments over a period of 4-16 weeks. Prior to enrolment in the study there will be a Pre-screening telephone call in order to assess key eligibility criteria.
Participants will be assessed at the following time points:
Visit 1. Screening (-70 to -14 days)
Visit 2. Baseline (telephone appointment) (Day 0): Randomisation
Visit 3. Day of Surgery (Day 10 - Day 21)
Visit 4. Post-surgery follow-up (telephone appointment*) (Day of Surgery + 7-21 days)
*A face to face visit for follow-up pregnancy testing will be required for women of child bearing potential

A computerised randomised system will be used for allocation of participants, to ensure equipoise.

Timeline for the study
Recruitment will be active for 18 months followed by a 4 week follow-up period until the final participant's study follow-up appointment.

Participant experience
There are two study visits plus two telephone appointments over a period of 4-16 weeks. Visits will take place at the participating hospital site. Two of the four appointments are routine NHS hospital visits with additional study procedures.
Blood tests will be taken at Visit 1 (Screening) and Visit 3 (Day of Surgery). At Visit 1 there will be a hand examination including measures of hand function. Questionnaires will be completed at Visit 2 (Baseline), Visit 3 (Day of Surgery), and Visit 4 (Post-surgery follow-up).
Participants will be asked to score the severity of their hand pain daily for up to 4 weeks prior to their trapeziectomy.

_____

Previous interventions:

RAMBOH-1 is a 2-arm double-blind randomised controlled proof of concept study using a pharmacological intervention. The study will take place in selected UK NHS hospitals, which will perform all study activities from recruitment to provision of intervention and follow-up.

Participants are randomised 1:1 to either talarozole or placebo. The dosing regimen is 2 capsules (2 x 1mg capsules of talarozole / 2 placebo capsules) are to be taken orally, once a day in the morning for 14 days prior to surgery (with day of surgery being day 14).

There are two study visits plus two telephone appointments over a period of 4-16 weeks. Prior to enrolment in the study there will be a Pre-screening telephone call in order to assess key eligibility criteria.
Participants will be assessed at the following time points:
Visit 1. Screening (-70 to -14 days)
Visit 2. Baseline (telephone appointment) (Day 0): Randomisation
Visit 3. Day of Surgery (Day 10 - Day 21)
Visit 4. Post-surgery follow-up (telephone appointment*) (Day of Surgery + 7-21 days)

*A face to face visit for follow-up pregnancy testing will be required for women of child bearing potential

A computerised randomised system will be used for allocation of participants, to ensure equipoise.

Timeline for the study
Recruitment will be active for 24 months followed by a 4 week follow-up period until the final participant's study followup appointment.

Participant experience
There are two study visits plus two telephone appointments over a period of 4-16 weeks. Visits will take place at the participating hospital site. Two of the four appointments are routine NHS hospital visits with additional study procedures.

Blood tests will be taken at Visit 1 (Screening) and Visit 3 (Day of Surgery). At Visit 1 there will be a hand examination including measures of hand function. Questionnaires will be completed at Visit 2 (Baseline), Visit 3 (Day of Surgery), and Visit 4 (Post-surgery follow-up).
Participants will be asked to score the severity of their hand pain daily for up to 4 weeks prior to their trapeziectomy.
They will be given the choice of using their personal smartphones (using a secure weblink presented in an SMS message, sent by the study database) or a paper diary.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Current primary outcome measure:
The difference in mean cartilage expression of a panel of pre-defined inflammatory gene mRNA levels (including, but not limited to ADAMTS4, MMP13 and MMP1) when comparing the intervention and placebo arms using a tissue sample collected at Visit 3 Day of Surgery

———

Previous primary outcome measure:
Mean cartilage expression of a panel of pre-defined atRA-responsive genes mRNA levels (including, but not limited to CYP19A, CYP26A, RARα, RARβ, and RARγ) using a tissue sample collected at Visit 3 Day of Surgery

Key secondary outcome(s))
Current secondary outcome measures as of 05/01/2024:
1. Mean levels of cartilage expression of atRA associated genes (including, but not limited to CYP19A, CYP26A, RARα, RARβ, and RARγ) using a tissue sample collected at Visit 3 Day of Surgery
2. Mean levels of cartilage expression of atRA responsive or inflammatory response genes when

considering ALDH1A2 genotype using a tissue sample collected at Visit 3 Day of Surgery
3. Mean levels of Synovial fluid and blood (plasma and cellular) molecular outcomes which may include inflammatory genes and response proteins, retinoic acid and drug levels using synovial fluid collected from the thumb CMC joint where available at Visit 3 Day of Surgery prior to excision of joint and blood samples collected at Visit 1 Screening and Visit 3 Day of Surgery.
4. Average daily hand pain on numerical rating scale (NRS), recorded by paper diary for up to 4 weeks ahead of surgery
5. Patient Evaluation Measure (PEM) at Visit 1 Screening, Visit 2 Baseline (Day 0) and at Visit 3 Day of Surgery visit (immediately before surgery)
6. Quality of life (EQ-5D-5L) at Visit 1 Screening, Visit 2 Baseline (Day 0) and at Visit 3 Day of Surgery visit (immediately before surgery)
7. Recruitment and randomisation rates using study records until end of randomisation
8. Acceptability to patients (% dropouts), collected throughout the study
9. Acceptability of study medication assessed by End of Study questionnaire and adverse events (AEs) at Visit 4 Post-surgery follow-up (at 4 weeks) and Safety Reporting Window

---

Previous secondary outcome measures:
1. Mean levels of cartilage expression of inflammatory response genes (including, but not limited to HAS1, IL6, NGF, and ADAMTS4) using a tissue sample collected at Visit 3 Day of Surgery
2. Mean levels of cartilage expression of atRA responsive or inflammatory response genes when considering ALDH1A2 genotype using a tissue sample collected at Visit 3 Day of Surgery
3. Mean levels of synovial fluid molecular outcomes which may include Inflammatory response proteins, retinoic acid and drug levels using synovial fluid collected from the thumb CMC joint where available at Visit 3 Day of Surgery prior to excision of joint
4. Mean levels of a panel of proteins in plasma using blood samples collected at Visit 1 Screening and Visit 3 Day of Surgery
5. Mean levels of gene expression from whole blood of a panel of atRA-dependent and inflammatory genes using blood samples collected at Visit 1 Screening and Visit 3 Day of Surgery
6. Average daily hand pain on numerical rating scale (NRS), recorded by daily online reporting or paper diary for up to 4 weeks ahead of surgery
7. Patient Evaluation Measure (PEM) at Visit 1 Screening, Visit 2 Baseline (Day 0) and at Visit 3 Day of Surgery visit (immediately before surgery)
8. Quality of life (EQ-5D-5L) at Visit 1 Screening, Visit 2 Baseline (Day 0) and at Visit 3 Day of Surgery visit (immediately before surgery)
9. Recruitment and randomisation rates using study records until end of randomisation
10. Acceptability to patients (% drop outs), collected throughout the study
11. Acceptability of study medication assessed by End of Study questionnaire and adverse events (AEs) at Visit 4 Post-surgery follow-up (at 4 weeks) and Safety Reporting Window

Completion date
30/06/2026

Eligibility

Key inclusion criteria
1. Participant is able to understand English and is willing and able to give written informed consent for participation in the study including to provide blood samples and donate tissue sample at surgery
2. Male or female, aged 18 to 75 years - updated 17/02/2025: aged 18-79 years

3. Symptomatic and radiographic thumb carpometacarpal (CMC) joint osteoarthritis scheduled for trapeziectomy surgery as part of usual care
4. Female participants fulfil either of these criteria:
4.1 Are of nonchildbearing potential, defined as:
- Aged 45 or over and definitely postmenopausal (defined as > = 2 years without any menses) prior to screening OR
- Documented as surgically sterile
4.2 Are of childbearing potential and fulfil all four of these criteria as well as the fifth, where relevant:
- Are not pregnant and have a negative pregnancy test at screening, and
- Agree not to try to become pregnant during the study and for 33 days after the final study medication administration, and
- Agree not to breastfeed from screening until 33 days after the final study medication administration.
- Agree not to donate ova from screening until 33 days after the final study medication administration.
- If heterosexually active, agree to consistently use one form of highly effective birth control from screening until 33 days after the final study medication administration.
5. Male participants fulfil both of these criteria:
5.1 They and their female spouse/partner(s) who are of childbearing potential agree to use 1 form of highly effective birth control from screening until 93 days after the final study medication administration.
5.2 They agree not to donate sperm from screening until 93 days after the final study medication administration.
6. The participant agrees not to consume grapefruit or grapefruit juice for the duration of the study
7. In the Investigator’s opinion, is able and willing to comply with all study requirements

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
79 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 25/06/2025:

1. Other cause of hand pain including inflammatory arthritis (such as rheumatoid arthritis, psoriatic arthritis, gout)
2. Use of one or more prohibited treatments within specified timeframe prior to screening, or not willing to avoid treatment for the duration of the study and for 75 hours after last dose:
In the last 3 years:
2.1 The retinoid medicine acitretin
In the last 3 months:
2.2. Retinoids (other than acitretin) or preparations containing high doses of vitamin A
2.3. Systemic immunomodulatory therapy (including systemic corticosteroids, methotrexate, sulfasalazine, hydroxychloroquine or cyclosporin)
In the last 6 weeks:
2.4. Initiation of or change to systemic hormone replacement therapy (HRT) or the combined oral contraceptive pill
2.5. Intra-articular steroid injection to the thumb CMC joint scheduled to undergo surgery
Currently receiving treatment with:
2.6. the following anticonvulsants: phenytoin, carbamazepine, oxcarbazepine, phenobarbital and other barbiturates
2.7. the following antifungals: ketoconazole, itraconazole, voriconazole, fluconazole
2.8. the following anti-retrovirals: ritonavir, indinavir, saquinavir, nelfinavir, efavirenz, nevirapine
2.9. the following antibiotics: erythromycin, telithromycin, troleandomycin, clarithromycin; rifampicin, rifabutin, isoniazid
2.10. the following calcium channel blockers: mibefradil, verapamil, diltiazem
2.11. coumarin anticoagulants including warfarin
2.12. certain antiemetics: netupitant, aprepitant
2.13. the following diabetic therapies: pioglitazone, troglitazone
2.14. the following antidepressants: nefazodone, St John's wort
2.15. the following other agents: conivaptan, modafinil
3. Presence of one or more medical contraindications to the use of talarozole or placebo:
3.1. Known hypersensitivity to drug or excipients in active medication or placebo (gelatin, polyethylene glycol (PEG) 400, PEG 4000)
3.2. Liver function tests (any of alanine aminotransferase (ALT), total bilirubin, alkaline phosphatase) > 1.5 times the upper limit of normal at screening or within 4 weeks of screening¥ orhistory of underlying disorder likely to affect liver function during the study (not including gallbladder disease).
3.3. Estimated glomerular filtration rate of < 60 mL/min per 1.73 m^2 at screening or within 4 weeks of screening¥ or history of underlying disorder likely to affect renal function during the study
3.4 History of low impact fracture (defined here as a fracture occurring spontaneously, or from a fall no greater than standing height, affecting wrist, hip or spine) or a known diagnosis of osteoporosis
3.5 Addison's disease or any other cause of clinically significant hypoadrenalism
3.6 Known infection with Human Immunodeficiency Virus
4. Excessively elevated blood lipid levels (a fasting total cholesterol/HDL ratio of >6.0 mmol/L or a fasting triglyceride level of >3.5 mmol/L)¥ or commensurate increases in non-fasting levels
5. Bone marrow disorder or clinically significant abnormality on full blood count at screening or within 4 weeks of screening¥.
6. Chronic pancreatitis
7. Active malignancy or a history of malignancy (except for treated nonmelanoma skin cancer) within the past 5 years, OR any form of chemotherapy.
8. Recent history of active cardiovascular disease (within the last 12 months) including clinically significant arrhythmias, symptomatic ischaemic heart disease, myocardial infarction or heart

failure (excluding effectively controlled hypertension or treated ischaemic heart disease which is clinically stable in the investigator's opinion)
9. Clinically significant abnormality on 12-lead electrocardiogram (ECG) performed within 3 months of screening
10. Uncontrolled hypertension (or supine diastolic blood pressure greater than 95 mmHg or systolic pressure greater than 160 mmHg at Screening Visit). These assessments can be repeated once, after a reasonable time period at the investigator's discretion. If the repeat exceeds one or more of these criteria, the patient will be excluded.
11. Uncontrolled diabetes mellitus (an HBA1c measurement of >8.0%)
12. Current psychosis, or other uncontrolled or clinically significant psychiatric disorder, including any significant risk to commit suicide, as judged by the Investigator and C-SSRS questionnaire.
13. Body mass index >39.9 kg/m²
14. History of alcohol or drug abuse/dependence/misuse within 1 year prior to screening.
15. Participation in another interventional study within the last 3 months, or treatment with an investigational drug within 1 month or 5 half-lives (whichever is longer) of Baseline.
16. Any other significant or uncontrolled disease or disorder which, in the opinion of the Investigator, may either put the participant at risk because of participation in the study, or may influence the result of the study, or the participant's ability to participate in the study
¥ These assessments can be repeated once, after a reasonable time period at the investigator's discretion (but within the screening period).

———

Previous exclusion criteria as of 05/01/2024:

1. Other cause of hand pain including inflammatory arthritis (such as rheumatoid arthritis, psoriatic arthritis, gout)
2. Use of one or more prohibited treatments within specified timeframe prior to screening, or not willing to avoid treatment for the duration of the study and for 75 hours after last dose:
In the last 3 months:
2.1. Retinoids or preparations containing high doses of vitamin A
2.2. Systemic immunomodulatory therapy (including systemic corticosteroids, methotrexate, sulfasalazine, hydroxychloroquine or cyclosporin)
In the last 6 weeks:
2.3. Initiation of or change to systemic hormone replacement therapy (HRT) or the combined oral contraceptive pill
2.4. Intra-articular steroid injection to the thumb CMC joint scheduled to undergo surgery
Currently receiving treatment with:
2.5. the following anticonvulsants: phenytoin, carbamazepine, oxcarbazepine, phenobarbital and other barbiturates
2.6. the following antifungals: ketoconazole, itraconazole, voriconazole, fluconazole
2.7. the following anti-retrovirals: ritonavir, indinavir, saquinavir, nelfinavir, efavirenz, nevirapine
2.8. the following antibiotics: erythromycin, telithromycin, troleandomycin, clarithromycin; rifampicin, rifabutin, isoniazid
2.9. the following calcium channel blockers: mibefradil, verapamil, diltiazem
2.10. coumarin anticoagulants including warfarin
2.11. certain antiemetics: netupitant, aprepitant
2.12. the following diabetic therapies: pioglitazone, troglitazone
2.13. the following antidepressants: nefazodone, St John's wort
2.14. the following other agents: conivaptan, modafinil
3. Presence of one or more medical contraindications to the use of talarozole or placebo:

3.1. Known hypersensitivity to drug or excipients in active medication or placebo (gelatin, polyethylene glycol (PEG) 400, PEG 4000)
3.2. Liver function tests (any of alanine aminotransferase (ALT), total bilirubin, alkaline phosphatase) > 1.5 times the upper limit of normal at screening or within 4 weeks of screening¥ orhistory of underlying disorder likely to affect liver function during the study (not including gallbladder disease).
3.3. Estimated glomerular filtration rate of < 60 mL/min per 1.73 m^2 at screening or within 4 weeks of screening¥ or history of underlying disorder likely to affect renal function during the study
3.4 History of low impact fracture (defined here as a fracture occurring spontaneously, or from a fall no greater than standing height, affecting wrist, hip or spine) or a known diagnosis of osteoporosis
3.5 Addison's disease or any other cause of clinically significant hypoadrenalism
3.6 Known infection with Human Immunodeficiency Virus
4. Excessively elevated blood lipid levels (a fasting total cholesterol/HDL ratio of >6.0 mmol/L or a fasting triglyceride level of >3.5 mmol/L)¥ or commensurate increases in non-fasting levels
5. Bone marrow disorder or clinically significant abnormality on full blood count at screening or within 4 weeks of screening¥.
6. Chronic pancreatitis
7. Active malignancy or a history of malignancy (except for treated nonmelanoma skin cancer) within the past 5 years, OR any form of chemotherapy.
8. Recent history of active cardiovascular disease (within the last 12 months) including clinically significant arrhythmias, symptomatic ischaemic heart disease, myocardial infarction or heart failure (excluding effectively controlled hypertension or treated ischaemic heart disease which is clinically stable in the investigator's opinion)
9. Clinically significant abnormality on 12-lead electrocardiogram (ECG) performed within 3 months of screening
10. Uncontrolled hypertension (or supine diastolic blood pressure greater than 95 mmHg or systolic pressure greater than 160 mmHg at Screening Visit). These assessments can be repeated once, after a reasonable time period at the investigator's discretion. If the repeat exceeds one or more of these criteria, the patient will be excluded.
11. Uncontrolled diabetes mellitus (an HBA1c measurement of >8.0%)
12. Current psychosis, or other uncontrolled or clinically significant psychiatric disorder, including any significant risk to commit suicide, as judged by the Investigator and C-SSRS questionnaire.
13. Body mass index >39.9 kg/m^2
14. History of alcohol or drug abuse/dependence/misuse within 1 year prior to screening.
15. Participation in another interventional study within the last 3 months, or treatment with an investigational drug within 1 month or 5 half-lives (whichever is longer) of Baseline.
16. Any other significant or uncontrolled disease or disorder which, in the opinion of the Investigator, may either put the participant at risk because of participation in the study, or may influence the result of the study, or the participant's ability to participate in the study
¥ These assessments can be repeated once, after a reasonable time period at the investigator's discretion (but within the screening period).

———

Previous exclusion criteria:

1. Other cause of hand pain including inflammatory arthritis (such as rheumatoid arthritis, psoriatic arthritis, gout)
2. Use of one or more prohibited treatments within specified timeframe prior to screening, or

not willing to avoid treatment for the duration of the study and for 75 hours after last dose:
In the last 3 months:
3. Retinoids or preparations containing high doses of vitamin A
4. Systemic immunomodulatory therapy (including systemic corticosteroids, methotrexate, sulfasalazine, hydroxychloroquine or cyclosporin)
In the last 6 weeks:
5. Initiation of or change to systemic hormone replacement therapy (HRT) or the combined oral contraceptive pill
6. Intra-articular steroid injection to the thumb CMC joint scheduled to undergo surgery
7. Currently receiving treatment with:
7.1. the following anticonvulsants: phenytoin, carbamazepine, oxcarbazepine, phenobarbital and other barbiturates
7.2. the following antifungals: ketoconazole, itraconazole, voriconazole, fluconazole
7.3. the following anti-retrovirals: ritonavir, indinavir, saquinavir, nelfinavir, efavirenz, nevirapine
7.4. the following antibiotics: erythromycin, telithromycin, troleandomycin, clarithromycin; rifampicin, rifabutin, isoniazid
7.5. the following calcium channel blockers: mibefradil, verapamil, diltiazem
7.6. coumarin anticoagulants including warfarin
7.7. certain antiemetics: netupitant, aprepitant
7.8. the following diabetic therapies: pioglitazone, troglitazone
7.9. the following antidepressants: nefazodone, St John's wort
7.10. the following other agents: conivaptan, modafinil
8. Presence of one or more medical contraindications to the use of talarozole or placebo:
9. Known hypersensitivity to drug or excipients in active medication or placebo (gelatin, polyethylene glycol (PEG) 400, PEG 4000)
10. Liver function tests (any of alanine aminotransferase (ALT), total bilirubin, alkaline phosphatase) > 1.5 times the upper limit of normal at screening or within 4 weeks of screening¥. OR
11. History of underlying disorder likely to affect liver function during the study (not including gallbladder disease).
12. Estimated glomerular filtration rate of < 60 mL/min per 1.73 m^2 at screening or within 4 weeks of screening¥. OR
13. History of underlying disorder likely to affect renal function during the study
14. Excessively elevated blood lipid levels (a fasting total cholesterol/HDL ratio of >6.0 mmol/L or a fasting triglyceride level of >3.5 mmol/L)¥ or commensurate increases in non-fasting levels
15. Bone marrow disorder or clinically significant abnormality on full blood count at screening or within 4 weeks of screening¥.
16. Chronic pancreatitis
17. Active malignancy or a history of malignancy (except for treated nonmelanoma skin cancer) within the past 5 years, OR any form of chemotherapy.
18. Recent history of active cardiovascular disease (within the last 12 months) including clinically significant arrhythmias, symptomatic ischaemic heart disease, myocardial infarction or heart failure (excluding effectively controlled hypertension or treated ischaemic heart disease which is clinically stable in the investigator's opinion)
19. Clinically significant abnormality on 12-lead electrocardiogram (ECG) performed within 3 months of screening
20. Uncontrolled hypertension (or supine diastolic blood pressure greater than 95 mmHg or systolic pressure greater than 160 mmHg at Screening Visit). These assessments can be repeated once, after a reasonable time period at the investigator's discretion. If the repeat exceeds one or more of these criteria, the patient will be excluded.
21. Uncontrolled diabetes mellitus (an HBA1c measurement of >8.0%)
22. Current psychosis, or other uncontrolled or clinically significant psychiatric disorder,

including any significant risk to commit suicide, as judged by the investigator
23. Body mass index >39.9 kg/m²
24. History of alcohol or drug abuse/dependence/misuse within 1 year prior to screening.
25. Participation in another interventional study within the last 3 months, or treatment with an investigational drug within 1 month or 5 half-lives (whichever is longer) of Baseline.
26. Any other significant or uncontrolled disease or disorder which, in the opinion of the Investigator, may either put the participant at risk because of participation in the study, or may influence the result of the study, or the participant's ability to participate in the study

¥ These assessments can be repeated once, after a reasonable time period at the investigator's discretion (but within the screening period).

Date of first enrolment
04/01/2024

Date of final enrolment
31/05/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Nuffield Orthopaedic Treatment Centre
Windmill Road
Headington
Oxford
England
OX3 7LD

Study participating centre
Heatherwood Hospital
Brook Avenue
Ascot
England
SL5 7GB

Study participating centre
Stoke Mandeville Hospital NHS Trust
Mandeville Road

Aylesbury
England
HP21 8AL

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

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?

HRA research summary			20/09/2023	No	No
Participant information sheet	version 1.0	16/08/2021	15/02/2022	No	Yes
Participant information sheet	version 3.0	24/08/2023	05/01/2024	No	Yes
Participant information sheet	version 4.0	27/03/2024	12/12/2024	No	Yes
Participant information sheet	version 5.0	29/10/2024	17/02/2025	No	Yes
Participant information sheet	version 6.0	12/05/2025	26/08/2025	No	Yes
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