Chief Investigator: Professor Dominic Furniss
Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford
Windmill Road, Headington, OX3 7LD.

RAMBOH-1

Retinoic Acid Metabolism Blocking agents to treat Osteoarthritis of the Hand

PARTICIPANT INFORMATION LEAFLET

We'd like to invite you to take part in our research study. Before you decide whether to take part, it is important that you understand why the research is being done and what it will involve. Please take time to read this information and discuss it with others if you wish. *If there is anything that is not clear, or if you would like more information, please ask us.*

What is the purpose of the study?

- Hand osteoarthritis (OA) is a common condition, however at present there is no proven treatment that prevents OA progressing.
- Recent research has shown that some individuals with severe hand OA have variation in a particular gene. This variation may lead to reduced production of a substance called retinoic acid (a natural anti-inflammatory agent). This decrease in retinoic acid may contribute to the progression of hand OA.

- Work in our laboratories has found that a drug called talarozole, which is an example of a Retinoic Acid Metabolism Blocking Agent (RAMBA), may help to prevent breakdown of retinoic acid and have an anti-inflammatory effect in OA.
- We want to test whether taking daily talarozole capsules by mouth for around 14 days before trapeziectomy (base of thumb surgery) can increase retinoic acid levels and reduce inflammation in the base of the thumb joint, when compared with taking a placebo capsule (inactive medication). To do this, we will measure changes in joint-based cell markers in spare tissue collected during your planned hand surgery which would normally be discarded.

- The study will generate information to tell us whether this drug is sufficiently promising to consider the planning of a larger clinical trial testing its use as a treatment for hand OA in the future.
- Talarozole has been used in clinical trials for other conditions but does not have a current license for use in hand OA or any other medical conditions.

Why have I been invited?

You have been invited to participate in this study because you have been scheduled for a trapeziectomy procedure for base of thumb OA. We need about 44 men or women aged 18-75 to take part in the study.

Do I have to take part?

It is up to you whether or not you take part. To take part you will be asked to sign a consent form. You are still free to stop taking part without giving a reason. Deciding not to take part, or to stop, will not affect your planned surgery or other treatment you are receiving or will receive in the future.

What will happen to me if I decide to take part?

First, we will explain the study to you and answer any questions you might have. We will then ask you for your verbal consent to allow us to initially assess, during a Pre-screening telephone call, whether you are suitable to join the study. We will ask you questions over the phone about your current health and medical history. As long as we don't identify a reason that would stop you taking part, we will invite you to a face-to-face screening (Visit 1) at *<insert site here>* where we will ask for your written consent to take part in the study before performing some further checks and procedures including blood tests. We will contact you following receipt and review of your blood results to confirm your eligibility.

If everything is OK with these further checks, we will then speak to you again over the phone (Visit 2) approximately 2 weeks before your scheduled surgery. During this call a computer will randomly allocate you to either the study medication (talarozole, a type of RAMBA) or the inactive medication (placebo). You have an equal chance of being allocated to either group. Neither you nor your doctors can choose whether you get the drug or know what you are given.

We will ask you to collect your allocated study medication from the hospital pharmacy and ask you to take it every day after this telephone call up to and including the day of your surgery (which will be for between 10 and 21 days). We will then see you at the hospital for study assessments on the day of your surgery (Visit 3) and follow up with you over the phone 2 weeks after surgery (Visit 4).

The Study Visits Schedule on the next page shows when the visits are and what will happen at each one. The timing of your surgery determines how long you will be in the study for (Visit 1 - Visit 4). This will be between 4 and 16 weeks, however all participants will take study medication for about the same number of days regardless of how long you are in the study.

Study Visit Schedule

Visit details	What will happen?
Telephone call **Pre-screening** ***Up to 50 minutes***	• Discussion of the study • Verbal consent for collection of information from medical notes • Collection of medical history and initial eligibility assessment
Hospital visit **Visit 1: Screening (At pre-operative assessment clinic where possible OR separate research visit)** ***Up to 2 hours***	• Consent to take part • Confirmation of demographic and medical information* • Physical examination • Measurement of blood pressure, pulse, height and weight • Electrocardiogram (ECG) (if you have not had one within 3 months) • Hand assessment including grip strength and pinch test measurements (see further information below this table) • Screening blood tests and urine sample (see: What will happen to the samples I give?) • Training in how to score daily hand pain & complete diary* (see further information below this Table) • A short questionnaire to assess aspects of your mental health **If COVID-19 restrictions require, these procedures may be carried out by telephone before this visit.*
13 days before Visit 2	• Start daily hand pain diary
Day before Visit 2	• Completion of study questionnaires on hand health/function and overall health (online or paper)
Telephone call **Visit 2: Baseline** ***Up to 30 minutes***	• Health and medication review • Allocation by computer to study medication • Instructions on how to take study medication After the appointment we will ask you to collect your study medication from the hospital pharmacy (instructions will be given at the time), or it may be possible for this to be sent to you by courier in exceptional circumstances
Approx. 13 days before Visit 3 (Day of Surgery)	• Take study medication daily • Continue/re-start daily hand pain diary • Start daily medication diary
Day before Visit 3	• Completion of study questionnaires on hand health/function and overall health (online or paper)
Hospital visit **Visit 3: Day of Surgery** ***Up to 45 minutes***	<u>Before your surgery:</u> • Health and medication review including mental health questionnaire • Additional study blood tests • Urine sample for pregnancy testing (where indicated) <u>During your planned surgery:</u> • Removal of fluid from your thumb joint using a needle and syringe (this fluid would normally be washed out during surgery) • Collection of bone and cartilage from your thumb joint (normally discarded during surgery)
Day before Visit 4	• Completion of study questionnaire on your opinion of the study medication (online or paper)

Telephone call^	
Visit 4: Post-surgery follow-up **1-3 weeks after surgery** ***Up to 30 minutes***	• Health and medication review including mental health questionnaire. • Urine sample for pregnancy testing (where indicated)^ *^Where applicable, a clinic visit may be required for pregnancy testing*

Further information on study procedures

- **Blood testing:** At Visit 1, we would like to take up to 35 ml of blood (equivalent to 2 tablespoons) for testing to check you are suitable to take part in the study. On the day of your surgery during study Visit 3, usually before you are taken to theatre, we would like to take another 35 ml of blood. This is a total of 70 ml (4 tablespoons) of blood during the course of the study. Please see Error! Reference source not found. for further information on the tests that will be carried out on your samples.
- **Hand assessments:** To understand your current level of function and strength in your hands we will carry out the following tests at Visit 1:
  - **Grip strength test:** You will be asked to squeeze a device in your hand to test your overall hand grip strength. We will ask you to hold and squeeze this device three times in each hand.
  - **Key pinch test:** You will be asked to squeeze in each hand a strength gauge between your thumb and index finger, specifically to measure the strength of your thumb.
- **Diaries**

  - **Hand pain diary:** We will ask you to record your average daily hand pain (on a scale of 0-10) in the 14 days leading up to your study Visit 2 and the 14 days leading up to your surgery (study Visit 3) on a paper diary.
  - **Medication diary:** Once you have started your study medication, we will ask you to record each day whether you have taken it or not on a paper diary.
  - Any paper diaries will need to be brought to the next study visit or posted to the study team in a pre-paid envelope. You will receive further information on this when you join the study.
- **Questionnaires:**
  - At Visit 2 we will ask you to complete 2 questionnaires on hand health/function and your overall health. You will be able to complete these online via an email link, or we can post these to you if you prefer. We will supply a pre-paid envelope for you to post these back to the study team. In the 24 hours before your Visit 3 (Day of Surgery), we will ask you to complete these same 2 questionnaires again.
  - Brief mental health questionnaire: in trials of new drugs, it is usual to routinely check for any significant mental health symptoms before and then during the trial. For this reason, at Visit 1 we will ask you a few questions about your mental health and whether you have ever had any thoughts about suicide. We will ask you these same questions at Visit 3 and Visit 4 to check whether anything has changed from Visit 1.
  - The day before Visit 4 (Telephone post-surgery follow-up) we will ask you to complete a final questionnaire about your experience of taking part in the study. This can be completed either online or on paper and returned to us by post.

What do I need to know about the medicine used in this study?

Talarozole is a type of Retinoic Acid Metabolism Blocking Agent. Talarozole has been tested by others in more than two hundred people taking part in clinical trials for skin conditions such as psoriasis and acne or in healthy volunteers. It is not currently a licensed medication for these conditions, or any other conditions. From this information, talarozole is generally well-tolerated but may cause some side effects.

Previously, when talarozole was given to around 90 people in the same way and at a similar dose to this study, no serious side-effects were recorded. Minor side effects included dry lips or skin, or soreness around the corners of the mouth, which occurred in 1 in 4 people. Less commonly, some people reported dry eyes, skin itching, skin irritation or hair loss. 1 in 10 people experienced an increase in their blood cholesterol or fats (triglycerides). For this reason, we check your blood fats as part of screening tests to check these are not very high, and then recheck these at Visit 3 after you have taken the study medication for around 14 days.

Based on the information we have, all of these issues would be expected to only occur in a minority of people, not be severe, and resolve after stopping the drug. We would expect lower numbers of side effects in this study as you will take the medication for a maximum of 21 days, compared to the other studies where people took the drug for 12-24 weeks, or at a higher dose.

It is important to know that you may experience none, some or all of the side effects described. In addition, there may always be side effects of the drug that are currently unknown because they are very uncommon. If you are concerned that you may have a side effect, you will be asked to contact the study team for advice or your doctor or 111/999 in an emergency. There is an option for the study doctor to recommend that you reduce (halve) the dose of medication in this circumstance or you may wish to stop the study medication altogether. Your safety will always come first.

We will also check blood tests when you finish taking the study medication, to check for any issues. No significant blood test problems are expected: we are doing this as a precaution and to give us more information about people with OA who are taking this medication.

How do I take the medication?

You will be prescribed study medication at Visit 2. You will be asked to take this daily for approximately 14 days (the exact timing may vary depending on when your surgery is scheduled) leading up to your trapeziectomy procedure. You should take two capsules, once a day in the morning, without regard to meals, and swallowed whole. Any capsules which you do not take you must bring back to the hospital when you come in for your Visit 3 (Day of Surgery) and give them back to the study team.

Should the date of your surgery change, a member of the study team will get in touch to explain what to do about taking your study medication. Depending on when your surgery will take place, you may be asked to continue taking the study medication (as 7 days of extra capsules will be provided) or you may need to stop and re-start at a later date. You will never take more than a total of 21 days of capsules altogether. It is not possible to supply you with

additional study medication; therefore, there may be circumstances where a change of surgery date could affect your participation in the study.

What should I consider?

Pre-existing or past conditions

There are some medical conditions, including conditions you may have had in the past that mean you would not be suitable to join the study. You will be asked about medical conditions or other reasons at Pre-screening and Visit 1 which would prevent you taking part. These include:

- Other cause for hand pain, including some types of inflammatory arthritis such as rheumatoid arthritis, psoriatic arthritis, and gout
- Bone marrow disorder
- Chronic pancreatitis
- Recent cancer (within 5 years)
- Recent or unstable heart condition
- Uncontrolled diabetes
- Liver or kidney disease
- Addison's disease or any other causes of insufficient adrenal hormones
- Osteoporosis or history of low impact bone fractures
- HIV positive status
- Very high levels of blood fats
- High or uncontrolled blood pressure
- High Body Mass Index (40 or over)
- Current active mental health problems, or past history of suicidal thoughts/actions

Current medications

You will be asked about your current medications and medication history at Pre-screening and Visit 1. There are some medications, and recent changes to medication that mean you would not be able to join the study. These include:

- Taking retinoids or preparations containing high doses of vitamin A in the last 3 months
- Taking immune suppressing medications such as steroids, methotrexate, sulfasalazine, hydroxychloroquine, or cyclosporine in the last 3 months
- Starting or changing certain types of hormone replacement therapy (HRT) or combined oral contraceptive pill (OCP) in the last 6 weeks (you can be on established HRT or OCP and take part in the study)
- Steroid injection to the thumb joint scheduled to undergo surgery in the last 6 weeks
- Some long-term antibiotics
- The blood thinning agent warfarin

You should continue your usual medications (prescribed and over-the-counter) during the study. We will record your medications at study visits and also ask that you tell us about any change in your usual pattern of use. We ask that whilst you are in the study, you try not to start new pain-relieving medications or steroid tablets and avoid vaccinations particularly whilst you are taking the study medication e.g., flu or COVID jabs as these things could affect the results of the study.

You are required not to consume grapefruit or its juice for the duration of the study, because it may affect the breakdown of the study medication.

You must not take part in any other clinical trials whilst you are in this study.

Contraception & pregnancy

Based on information available to us, talarozole could cause harm to an unborn baby or infant that is breastfed and could temporarily damage sperm. You or your partner should not become pregnant if participating in the study or for a period of time after the study (see below). It is important that you understand the study requirements for contraception to prevent pregnancy and what would happen if you or your partner become pregnant. Based on lack of information of this drug's effects in human pregnancy, we cannot give you an indication of how likely or unlikely a problem is with a pregnancy. Based on the mechanism of the drug and other testing it has undergone, problems are possible.

The study team are required to follow-up on any pregnancy that occurs in those that received talarozole or their partner, and we will ask for your specific consent for this when you join the study. It is important that we collect information from you/your partner to monitor any possible effects of talarozole on the outcome of the pregnancy. Please note that we are expected to collect this information even if you decide to stop participating in the study or have stopped taking the study medication.

Female participants:

- You will not be able to take part in the study if you are pregnant, intending to become pregnant in the coming months, or breastfeeding.
- Breastfeeding and the donation of eggs must not occur until 33 days after the final dose of study medication.
- If you could become pregnant, you will be tested to ensure that you are not pregnant before you join the study at Visit 1, and again at Visit 3 and Visit 4 to check that you have not become pregnant during the study. You must also use a highly effective method of contraception (see accepted methods on page 8) on joining the study through to 33 days after your final dose of study medication.
- In the unlikely event that you become pregnant whilst on study medication or within 33 days after the final dose, you must notify the study team as soon as possible. You will be asked to stop taking the study medication immediately if you haven't already. The study team will then check whether you were taking talarozole or placebo to decide on the next steps. If you received the placebo there will be no further action.
- If you did receive talarozole, we will then obtain information about your pregnancy, and in due course its outcome, directly from your and/or your child's medical records and may contact you to arrange an appointment if necessary, to collect additional information related to your pregnancy e.g., details such as date of your last menstrual period and your estimated date of delivery.

  We will ask you to notify us regarding the outcome of your pregnancy. If we don't hear from you within a week of your estimated date of delivery, we will contact you to ask about the outcome of your pregnancy. Depending on the outcome of your pregnancy, further information from your and/or your child's medical records may need to be collected for a period of time following this.

Male participants:

- Talarozole may damage sperm whilst you are taking it, but no longer-term fertility issues are anticipated (although as an additional precaution, we will monitor sex hormones on blood tests during the study). For this reason, pregnancies should be prevented during the study and for up to 93 days afterwards. This includes the donation of sperm.
- If you have a female partner who could become pregnant, you must use a highly effective method of contraception (see acceptable methods below) on joining the study through to 93 days after your final dose of study medication. In this situation, we request that you discuss your study participation with your partner, making them aware of the risks of any pregnancy, and the requirement of the study team to follow-up on any pregnancy that occurs during the study. We are happy to speak with your partner and you together about any aspect of this if you wish.
- If in the unlikely event that your partner becomes pregnant whilst you are taking study medication or within 93 days after the final dose, you must notify the study team as soon as possible. The study team will then check whether you were taking talarozole or placebo to decide on the next steps. If you received the placebo there will be no further action. If you received talarozole the study team will then contact your partner to obtain their consent to collect information on the pregnancy and its outcome. Information about such a pregnancy may be obtained direct from the mother's and/or child's medical records.

- **Highly effective methods of contraception include**:
  - Hormonal forms of contraception including;
    - Combined forms (estrogen and progestogen containing) such as the combined oral contraceptive pill (at a stable dose for at least 3 months before entering the study), patches, or vaginal rings
    - Progestogen only forms including the progestogen-only pill, injections, or implants
  - Intrauterine device/system
  - Sterilisation
  - Vasectomised partner
  - True sexual abstinence (refraining from heterosexual intercourse during the entire period of risk associated with the study medication)

Are there any possible disadvantages or risks from taking part?

- Participating in the study will take time, including on the day of your planned surgery. At the outset, you need to be confident that you are able to commit the time needed to attend study visits either via telephone or at clinic. Visits are carried out during normal office hours, and their timing is in consultation with you.
- Blood samples: When having your blood taken, minor bruising at the needle puncture site may occur in some people. Please tell us if you are worried about having blood taken.
- Medication: sometimes any form of medication can cause unwanted effects. You will be monitored for any possible side effects of the study medication during the study. The possible side effects that we know about are listed above in the **What do I need to know about the medicine used in this study?** section.

- During surgery, prior to opening the joint, synovial fluid from your thumb joint will be collected with a needle and syringe but there is no additional risk associated with this procedure over that of surgery.
- Taking part in the study is not expected to affect how your surgery will be performed or the risks or benefits associated with it.

What are the possible benefits of taking part?

There is no direct benefit to you from taking part in this study. We do not know what the outcome will be, which is why we are conducting the research. During the study you will be monitored closely by a doctor and this monitoring may have indirect health benefits. The study will give us useful information which may benefit others in the future and help the development of new treatments for OA.

The short duration of medication in this study is not expected to cause a substantial change in your OA or your need for hand surgery. It is to allow testing of whether the drug has the effect that we expect in the joint, which would enable us to run further clinical trials in the future.

In taking part in this study, you will help us to understand more about OA and its potential treatment.

Will my General Practitioner/family doctor (GP) be informed of my participation?

Taking part in the study could affect your clinical care. We will therefore ask for your consent for us to inform your GP that you are participating in the study.

Will my taking part in the study be kept confidential?

- Your identity as a participant in this study will be kept confidential. Study documents and data will only be accessible by the study team and authorised personnel.
- To help keep your information confidential, any information recorded about you in this study will be stored under a unique participant identification number. On some study documents it is necessary to add your initials as well, and the pre-screening form and your consent form will include your name.
- Because of the way the study is run, if you take part in the study, you need to agree to study team members at your hospital and central study team members at the University of Oxford having access to your identifiable details. This is only where necessary for study activity. For example, so we can send you the study questionnaires to complete.
- If you agree to complete study questionnaires by email, your name and email address will be held in a secure database (with access restricted to study team members) in order to facilitate this for the duration of the study and deleted after study results have been disseminated (a maximum of 3 years).
- Your participation in the study will be recorded in your NHS records at the relevant hospital.
- Identifiable information (name, hospital number, NHS number and date of birth) will be included on study related items such as prescriptions and blood samples that will not leave the hospital.

- Responsible members of the University of Oxford and the relevant NHS Trust may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.
- If you undergo Pre-screening for the study but do not take part because you do not want to or are not eligible, the hospital study team will keep information on your pre-screening for the purposes of the study (any identifiable information will be removed) unless you request to remove it.
- De-identified study data including on any serious side effects experienced, or reports of pregnancy whilst taking talarozole, will be shared by the study team with the company who manufactured the drug, GlaxoSmithKline (GSK), covered by an appropriate agreement.
- Some of your samples may be processed by third parties outside the University of Oxford. No personally identifiable information will be shared, just your study ID will be used link the samples to you.
- Following the end of the study we will create and store a de-identified data set which we may share with other researchers or collaborators (this may include commercial organisations), in the UK and abroad, including through a data repository. You could not be identified from this data. Sharing and storage of this data will continue for as long as this data is useful.

Will I be reimbursed for taking part?

You will not receive any payments for participating in the study, other than reimbursement for reasonable travel expenses to and from the hospital for study appointments only, i.e. visits that are for the purposes of the study only and not usual hospital appointments. Your travel costs will be reimbursed based on the receipts you provide, so please keep all your travel and parking receipts and tickets and/or a record of your mileage and give/post these to the study team. Unfortunately, we cannot pay for the travel of others who accompany you to appointments.

You should not incur any costs by participating in the study other than travel expenses, however if you feel you are incurring costs, please discuss this with the study team.

What will happen to the samples I give?

- At Visit 1 a blood sample and a urine sample will be taken. Blood samples will be sent to the NHS hospital laboratory for tests to check you are suitable to join the study, including a blood count, liver and kidney function tests, and sex hormone tests if you are male. A urine test will be analysed in the clinic to check that you are eligible to join the study (blood traces, glucose, and protein will be tested). For women of child-bearing age, we will also perform urine tests to exclude pregnancy (follow-up pregnancy tests will also be required at Visit 3 and Visit 4 where applicable). All urine samples will be destroyed immediately after testing.

- At Visit 3 we will take another blood sample which will include all of the relevant safety tests (to monitor your health whilst in the study). Male participants have their sex hormones tested again. These tests will be undertaken by the hospital laboratory and will be destroyed once the requested tests are complete (as per usual hospital policy).
- Separate blood samples from both of these visits will also be sent to our research centre, the Kennedy Institute of Rheumatology, at the University of Oxford, for exploratory tests including measurement of markers of inflammation.
- As part of your surgical procedure, a small bone in the base of your thumb (the trapezium) will be removed. Usually this would be discarded as waste tissue; however, if you take part in the study, we will ask the surgeon to keep the bone and send it to the Kennedy Institute of Rheumatology laboratories for testing. We will extract and store DNA and RNA from the bone and attached cartilage. This will allow us to use your DNA to find out which variants of the genes connected to hand OA severity that we are investigating you have and see if this affects how your cells have responded to the study medication. In the future we may do the same sort of tests for other genes relevant to this medication and OA. We are also interested in the cartilage that is attached to the bone and will test the RNA for a response to the study medication. At the time of your surgery, we may also collect up to 1ml of synovial fluid (the lubricating fluid that surrounds your joints) from the joint that is being operated on and analyse this in the same way.

- Samples sent to the Kennedy Institute laboratories will be labelled only with your study ID number, initials, and the date the sample was taken; these will be processed, then frozen and stored for analysis during the study or within 12 months of the end of the study.
- We may send some samples to external companies outside of the University for analysis. If this happens, no personally identifiable information will be shared, just your study ID will be used link the samples to you.
- We will ask for your consent to transfer any remaining samples at the end of the study for indefinite storage in a registered Research Tissue Bank in Oxford. From here, your anonymised samples may be used with the permission of the study team by ourselves and other local researchers, and also in ethically approved research projects in hospitals, universities, non-profit institutions or commercial laboratories worldwide. In this scenario, your samples would only be provided in a way that does not identify you; however, your DNA is unique to you so can never be completely anonymous.

What will happen to my data?

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of

Oxford is the data controller and is responsible for looking after your information and using it properly. We will be using information from you and your medical records in order to undertake this study and will use the minimum personally-identifiable information possible. We will keep identifiable information about you for a maximum of 3 years after the study has finished to let you know the results of the study. This excludes any research documents with personal information, such as consent forms which will be held securely at the University of Oxford for 5 years after the end of the study. If you agree to your details being held to be contacted regarding future research, we will retain a copy of your consent form until such time as your details are removed from our database but will keep the consent form and your details separate. If you agree to your samples being used in future research long-term (this is optional) your consent form will be held securely at the University of Oxford until the samples have been depleted or destroyed.

The local NHS Trust will use your name, NHS number, home address, and contact details, to contact you about the research study, and to oversee the quality of the study. They will keep identifiable information about you after the study has finished as per local Trust policy. A copy of your consent form will be stored in your electronic medical records permanently.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at https://compliance.web.ox.ac.uk/individual-rights.

You can find out more about how we use your information by contacting ramboh-1@kennedy.ox.ac.uk.

What will happen if I don't want to carry on with the study?

- Your participation in this research study is entirely voluntary. You are entitled to withdraw from the study at any time and will continue to receive the same standard of care from your doctors.
- If you withdraw from the study entirely, no further study visits will occur and no further samples or data will be collected but the study team will keep information and samples collected up to a point of withdrawal for the purposes of the study (any identifiable information will be removed). However, **if you have taken any amount of study medication, we will ask you to complete a short follow-up assessment to ensure your safety.**
- Should you decide or need to stop taking your study medication we would like you to continue in the study so that we can collect your data and samples, as this is useful to us. We will still collect your tissue at surgery in this case unless you withdraw from the study entirely.
- You must contact the study team using the contact details below if you wish to withdraw from the study and/or stop taking study medication.

What happens at the end of the study?

- During and after the study, your healthcare professional or GP will continue your usual care. This is independent from your participation in the study. If we identify any results obtained during the study that may affect your ongoing care, with your consent we will contact your GP to pass on this information.
- We will write to you at the end of the study (by post or email as per your preference) once we have the study results to give you a brief summary of what we found. We expect this will be within 12 months of the last participant completing the last visit but it may be longer. We will not be able to tell you whether you received talarozole or the placebo, unless unblinding takes place during or after your participation for medical reasons.
- We will publish the research in a scientific medical journal and present the findings at medical conferences. This can potentially take several years. Any information we publish, in any format, will never reveal your identity or contain any information that could be linked to you specifically.

What if we find something unexpected?

If we find anything unexpected, for example any medically significant information that may have implications for your clinical care, we would let you know and, with your consent, write to your GP.

What if there is a problem?

The University of Oxford, as Sponsor of the study, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment (your surgery and usual NHS care) which is provided.

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, you should contact <name of investigator><contact details (study phone number & study email)> or you may contact the University of Oxford Research Governance, Ethics and Assurance team (RGEA) office on 01865 616480, or the head of RGEA, email RGEA.Sponsor@admin.ox.ac.uk.

The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study.

If you wish to contact the PALS team, please contact <insert relevant NHS site phone number and email from the PALS website http://www.ouh.nhs.uk/patient-guide/pals.aspx>.

How have patients and the public been involved in this study?

Several patients with hand OA are involved in the design and delivery of the study, attending study oversight meetings and checking our progress. These patients were also involved in reviewing this participant information leaflet and other patient facing documents.

The study was also presented to a panel of patients with OA at the 2018 Research Showcase event, organised by the Centre for Osteoarthritis Pathogenesis Versus Arthritis, and there was an opportunity for discussion and feedback.

Who is organising and funding the study?

The study is sponsored by the University of Oxford and led by Professor Dominic Furniss (Chief Investigator) and Professor Tonia Vincent who are both musculoskeletal consultants and researchers. The study is run by a team based at the University of Oxford. The Medical Research Council is funding this study. The study also benefits from resources including staff time provided by the NIHR Biomedical Research Centre and the Centre for Osteoarthritis Pathogenesis Versus Arthritis, which are based in Oxford.

Neither your doctor nor the study team will benefit financially from you taking part in this study.

Talarozole is a drug owned by GSK and was developed by them. Talarozole has been donated by GSK to the University of Oxford for the purposes of the study at our request. Information on the drug has also been shared with us. GSK are not otherwise involved in the design, funding or delivery of this study but will receive de-identified study data for drug safety monitoring purposes.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by East Midlands - Nottingham 2 Research Ethics Committee.

Participation in future research

We will ask for your permission to add your contact details to the OsteoArthritis Research Volunteer Interested List (OARVIL) at the Centre for OA Pathogenesis Versus Arthritis in Oxford. By joining OARVIL, we can contact you about participation in relevant future research and other research involvement opportunities at the Centre. Your details will be held securely on the OARVIL database (separate from this study) with access restricted to authorised personnel. You are under no obligation to participate in any subsequent trial or other studies, and in each case, you would always need to provide formal consent to participate. You are free to withdraw your details from this list at any time.

What will happen to my data?

If you agree to your details being held to be contacted regarding future research, we will retain a copy of your consent form until such time as your details are removed from our database.

Further information and contact details

If you would like to join the study or have any questions about the study please contact <local coordinator/investigator> by <insert phone number and email>.

Thank you for taking the time to reading this information.