PATIENT INFORMATION SHEET

INSTITUTION HEADED PAPER

1. Study title
Towards A Cure for Early Rheumatoid Arthritis: The TACERA Study

2. Invitation paragraph
We would like to invite you to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

3. What is the purpose of the study?
Rheumatoid Arthritis (RA) is an inflammatory disease which affects the joints in the body. A number of treatments are available which aim to induce remission, a state in which the arthritis is inactive and patients are no longer experiencing symptoms. However, it is currently difficult to determine which treatment will work best for a particular patient, and patients are often required to try multiple therapies before finding a successful one.

We hope that a set of immunological tests forming a 'toolkit' could be developed to help us to predict which patients will respond well to particular treatments, the aim being to achieve disease remission where patients would no longer be experiencing active symptoms such as pain and swelling. In order to do this we need to capture information from patients before and during treatment for their Rheumatoid Arthritis.

The purpose of the study is to collect detailed clinical information and biological samples over an 18 month period that will enable investigation of clinical and immunological predictors of response to treatment and help us further understand the state of remission in rheumatoid arthritis.

4. Why have I been invited?
We are approaching you because you have recently been referred by your GP to a Rheumatology Outpatient Department for assessment of your arthritis. Depending on the outcome of this assessment, it is possible that you may be eligible to participate in this study.

5. Do I have to take part?
No. It is up to you to decide whether or not to take part. We will describe the study and go through this information sheet which we will then give to you. We will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care nor the treatment that you receive.

6. What will happen to me if I take part?
If you decide to take part in this study we will follow you over an 18 month period, collecting detailed information about the treatment of your arthritis and how you respond to it. To do this you will need to attend your rheumatology outpatient department every 3 months to have your arthritis assessed by a member of the research team. The frequency of assessments for this study have been designed to coincide with routine visits as recommended by NICE (National

Institute for Health and Clinical Excellence) whose guidance sets the standard for high quality health, social care and public health, including recommendations for the best treatments for patients.

We estimate that these visits will take approximately 1 to 1 ½ hours, and will consist of an assessment of your disease activity, completing questionnaires about how arthritis affects your daily life and collecting information on lifestyle factors since these are known to influence the risk of developing RA, as well as the response to therapy. Blood tests will also be performed during these visits. Some of the blood we take will be used for routine monitoring of the effects of the medication that you will be prescribed for your arthritis. Additional blood (between 60 and 120ml per visit, equivalent to 1.5 - 3 egg cups) will be taken to look at immunological and genetic markers, and urine samples will also be taken for laboratory analysis. Blood will be drawn every 3 months, so you will be asked to provide a total of 7 blood samples over the 18 month period of the study. The total volume will be equivalent to less than 1.5 pints of milk over the 18 month period.

In the unlikely event that blood and urine samples do not reach the laboratory for processing, or there is an unacceptable delay, we would like to ask if you would be willing to provide another sample for us. You will be under no obligation to do so. If you agree we will ask you to complete an additional consent form to provide another blood sample within an acceptable time frame, which is likely to be two weeks.

In some cases, your research nurse or rheumatologist may want to see you more regularly, especially in the first few months, to ensure the medication you have been prescribed is working. Similarly, you may also be telephoned by a research nurse between visits to check how you are feeling. Although the visits and calls will form part of routine care, we may collect any information recorded as part of the study.

The medication that you receive to treat your arthritis during the study period will be prescribed according to national guidelines. This treatment will not differ from that which would be prescribed if you choose not to enter the study. Changes to your medication during the study period will be made by your rheumatologist according to the national guidelines, where necessary, for the treatment of your arthritis. As this is an observational study (meaning that we are just looking at how your arthritis responds to standard therapy, rather than testing the effects of new treatments), your participation will not affect the medication you receive or the choices made by your rheumatologist.

7. Expenses and payments

Whether or not you take part in this study, as part of your rheumatoid arthritis care, you will need to attend routine follow up appointments in a rheumatology clinic for regular specialist advice. We would not be able to support you attending for these routine appointments if you weren't in the study, so there is no payment for attending these routine appointments whilst participating in the study. However, you will be able to claim up to £45 for additional expenses incurred during the course of the study (e.g. extra parking fees).

8. What will I have to do?

You will be asked to attend 7-8 assessments over 18 months whilst taking the medication prescribed by your rheumatologist. As mentioned previously, the study visits have been designed to coincide with routine visits.

In addition to routine x-rays, some of our study sites perform ultrasound scanning of affected joints. If you are seen at one of these sites you may be invited to undergo ultrasound scanning at your first appointment, and then at the 6, 12 and possibly 18 month assessments. This is a non-invasive procedure using a machine similar to that which monitors foetal growth during pregnancy.

You will not be allowed to participate in other studies which could potentially have an effect on your arthritis or treatment. However, you will be able to participate in other observational studies, including studies involving synovial biopsies, since these kinds of studies should not affect your arthritis or its treatment.

You can continue to take any additional medication, as directed by your doctor, either for arthritis or any other condition. You may consult your GP during the study with regards to your arthritis if appropriate. There are no other specific lifestyle changes needed.

9. What are the alternatives for diagnosis or treatment*?*
As stated above, this is an observational study, so the treatment you will receive as a participant in the study will not differ from what you would receive if you did not participate. You can discuss your treatment options with your rheumatologist at any point either before or during the study.

10. What are the possible disadvantages and risks of taking part?
As this is an observational study there are no additional risks relating to taking medication involved beyond those which you would experience in routine care. However, there is a modest risk of side effects including pain, bruising, light headedness, and, on rare occasions, infection that could arise as a consequence of having blood taken. To minimise this risk, blood will be taken by a clinical professional trained and experienced in taking blood from patients. In all we'll need to take 7 lots of blood samples from you, in total about 1.5 - 3 egg cups of blood on each occasion, during this study.

Although you would routinely attend follow up appointments as part of your rheumatoid arthritis care, you may have to attend for longer than normally expected in order to complete all the questionnaires and clinical assessments. You will be able to claim up to £45 during the course of the study for any additional expenses that may be incurred (e.g. extra parking fees).

11. Ionising Radiation (Medical Exposure) Regulations – IRMER
This study will involve having one additional set of hand and feet x-rays to normal clinical practice to see how your disease is progressing. Experts on ionising radiation have been consulted and have confirmed that this additional x-ray carries a negligible risk to you.

12. Harm to the unborn child: therapeutic studies
For women: almost all of the medications that you will receive to treat your arthritis whilst on this study might harm an unborn child. Therefore you should inform your rheumatologist if you are pregnant, breast-feeding or are likely to become pregnant during the study period. If you could become pregnant, you will be asked to have a pregnancy test (urine or blood) before taking part. You should be using a reliable form of contraception during the study, e.g. oral contraceptive and condom, intra-uterine device (IUD) and condom, diaphragm with spermicide and condom.

If you do become pregnant during the course of the study, we would ask you to tell your study doctor immediately so they can decide appropriate action. We would discuss referral for

specialist counselling on the possible risks to your unborn baby and arrangements will be offered to monitor the health of both yourself and your unborn baby.

For men: it is not known if the study medicine will affect sperm or semen and therefore you should not father a child while taking your arthritis medication without discussing the risks with your doctor. If your partner might become pregnant you must use reliable forms of contraception e.g. oral contraceptive and condom, intra-uterine device (IUD) and condom, diaphragm with spermicide and condom.

If your partner becomes pregnant while you are taking your arthritis medication, or within 6 months of stopping treatment, you should inform your doctor immediately. As the risk to your partner and baby is unknown, it is desirable for your partner to agree to medical supervision during her pregnancy and for the baby after it is born.

13. What are the possible benefits of taking part?
We cannot promise the study will help you but your arthritis will be monitored very closely by the rheumatology research team. You will have a dedicated research nurse who you will be able to contact directly with any questions or concerns relating to your care and also your participation in the study.

Additionally, although not a direct benefit to you as a result of participating in this study, it is hoped that the information we get from this study will help improve the treatment of people with rheumatoid arthritis in the future.

14. What happens when the research study stops?
Your rheumatologist will continue to monitor your arthritis according to national guidelines and local practices.

15. What will happen if I don't want to carry on with the study?
You can withdraw from the study at any time. If you decide to withdraw from the study, your standard of care will not be affected.

You will still need to attend for your routine follow-up assessments as part of your standard NHS care.

If you would be happy to do so, we would like to continue to collect information and samples from you at these less frequent follow up appointments. Whether you agree to this is completely up to you and will again not affect your standard of care should you decide that you wish to have no further participation in the study.

If you withdraw from the study, all samples and clinical information that we have obtained up to the point of you coming out of the study will continue to be used for the purpose of the study.

16. What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (Professor Cope, the Chief Investigator, can be contacted on 020 7848 6901).

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from your hospital.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against The NHS Trust administering your care but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

17. Will my taking part in this study be kept confidential?
Yes. We will follow ethical and legal procedures and all the information about your participation in this study will be kept confidential. If you join the study, some parts of your medical records and the data collected for the study will be looked at by the Chief Investigator (Professor Cope) or staff working under his supervision to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

All information that is collected about you during the course of the research will be kept strictly confidential, and any information about you that leaves the hospital/surgery will have your name and address removed so that you cannot be recognised.

18. Involvement of the General Practitioner/Family doctor (GP)
We will notify your GP about your involvement in the study. Your rheumatologist will also keep them informed about the treatment you are taking and any changes made during the study in line with current medical practice.

19. What will happen to any samples I give?
Your research nurse will take blood and collect a urine sample at each assessment and send them to a nearby laboratory. There, the samples will be either processed for analysis on the same day, or processed and subsequently sent for storage at the UK Biocentre, a Human Tissue Authority licensed storage facility (or Biobank) for human blood and tissue samples. Analyses on samples sent for storage will be carried out at a later stage to confirm and validate findings from initial laboratory test by study investigators or their designated collaborators. Some of your samples will be sent to expert processing laboratories where they will be analysed by the research team. Your samples will be anonymised and given a unique code so that they cannot be directly traced back to you as the donor by members of the laboratory research team. Your identity will be protected as this code will not be linked with your coded samples when the samples are analysed. However, the data collected from your samples will be linked with the clinical information you provide during the study to enable responses to treatment to be compared with immunological and genetic markers. It is this combination of clinical and laboratory data that will be used to develop the immunological toolkit.

As part of the process of safety monitoring of the treatment you receive, you will also be asked to give blood samples for use in the routine clinical management of your arthritis. Where possible, these will also be taken by your research nurse at your assessment to avoid the need for you to visit the hospital phlebotomy department or your GP practice. These samples will not be stored, but will be processed and analysed by the hospital clinical laboratory. The results will be stored on the hospital computer system along with any other tests you have had at your local hospital in the past, and will be reviewed by the doctor who is looking after you.

20. Will any genetic tests be done?
The samples taken at each assessment will be processed to look for immunological markers which will be used to develop the immunological toolkit. At the beginning of the study we will also take blood to look at genetic markers related to Rheumatoid Arthritis and its treatment. These samples will be sent to a facility in Manchester for analysis carried out by study

investigators or their designated collaborators. Any leftover samples will be sent to the UK Biocentre (a registered biobank) for long term storage. We hope that the toolkit will enable us to make patient specific treatment choices in the future and help us to predict which patients are most likely to enter remission if given a specific treatment. We would also like to use the samples to look at any new biomarkers or genes that are discovered in the future or analyse them with any new technologies that become available in relation to Rheumatoid Arthritis and its treatment.

21. What will happen to the results of the research study?
The overall results of the study will be collected together by the Chief Investigator and his staff who intend to present and publish the findings to inform others about which treatment to use. This will take at least 5 years from the beginning of the study. When the results are published we will be happy to make them available to all the patients who took part. We will only make available the overall results of the study.

No individual patient will be identified in any report or publication from this study.

22. Who is organising and funding the research?
This research is funded by the Medical Research Council and is administered by King's College London, where the Chief Investigator, Professor Andrew Cope, works.

23. 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 your safety, rights, wellbeing and dignity. This study has been reviewed and given a favourable opinion by NRES (National Research Ethics Service) Committee London - Central.

24. Patient Representatives
We have asked a patient with rheumatoid arthritis to help advise us on this study. This patient is known as a Patient Representative and their role is to advise the study's Steering and Data Monitoring Committee (a committee that makes decisions about the design and conduct of the study) from the patient perspective. If you would like to speak to a Patient Representative you can telephone the Study Office on 020 7848 5206 or email kch-tr.rheumatology-research@nhs.net and we will pass on your details.

25. Further information and contact details

For further information please contact:

Dr. (Local Researcher)

Telephone:

OR

Study Co-ordinator
King's Musculoskeletal Clinical Trials Unit
Academic Department of Rheumatology
School of Medicine
Weston Education Centre, Denmark Hill, London, SE5 9RJ
Telephone: 020 7848 5206 *(daytime)*

OR

Professor A Cope
Professor of Rheumatology
Academic Department of Rheumatology
CMCBI, DIIID, School of Medicine, 1st Floor New Hunt's House
Guy's Hospital Campus, Great Maze Pond, London, SE1 1UL

Telephone: 020 7848 6901 *during the normal working day.*

Outside the normal working day this number has an answer phone and your query will be dealt with as soon as possible.

In emergencies only, please contact the 24-hour study contact line, which is: 07590 045 407

You will be given a copy of this Patient Information Sheet and a signed consent form to keep. We would like to thank you for reading this form and for considering taking part in the study.