Participant Information Sheet
(Final version 4.0 17 July 2020)

IRAS Project ID: 263669

Title of Study: Treat-to-Target in gout

Name of Chief Investigator: Dr A Abhishek, Clinical Associate Professor of Rheumatology, University of Nottingham.

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you.

What is the purpose of this study?

Gout causes flares of severe joint pain and swelling. It occurs as a result of a high urate level in the blood which leads to urate crystals depositing in the joints. Medications such as allopurinol lower the blood urate levels and dissolve the urate crystals. This should lead to less frequent gout flares provided they are taken for long enough to dissolve the urate crystals.

Researchers at the University of Nottingham are conducting a study together with Keele University and the University of Southampton to look at the most effective way to prevent gout flares in people who have had gout. You will not be prescribed any new untested medications in this study. If you agree to participant in the study, you may be advised to take available treatments for gout such as allopurinol at a dose that is sufficiently high to help dissolve urate crystals in your joints.

The usual treatment of gout is to just treat each gout flare with anti-inflammatory medicines such as ibuprofen or to try and prevent flares of gout using urate-lowering medicines such as allopurinol at a fixed dose. This study will find out whether a gradual increase in the dose of urate-lowering medicines, guided by blood tests for urate levels, is better at preventing gout flares. Thus, the results of this study will improve the treatment of gout in the UK by finding the right way of managing gout in the long-term.

Why have I been invited?

You have been invited because your GP records show that you have gout or have previously been prescribed gout treatment, or you have expressed an interest in taking part in the study based on information that you have seen. Patients who fit these criteria are being invited to provide information about their gout by filling in a questionnaire to see whether the study is suitable for you. As part of this questionnaire, the research team are asking people if they would be willing to be contacted again regarding the next stage of the

study. We are recruiting approximately 466 patients to take part in the study in areas across the country.

Do I have to take part?

It is completely up to you to decide whether or not you would like to take part in this study. Whether you choose to take part or not will not affect your current or future health care in any way.

If you decide to take part, you are still free to withdraw from the study at any time and would not have to give a reason for this. This would not affect your legal rights. You can withdraw by contacting Keele Clinical Trials Unit on 01782 732950 or email sch-tr.t2tgout@nhs.net quoting the T2T study.

What next?

If you are interested in participating in the study, please complete the short questionnaire enclosed with this leaflet to see whether the study is suitable for you. Once completed, please return this questionnaire to the Keele Clinical Trials Unit in the self-addressed freepost envelope provided. **You do not need to attach any stamps.**

The research team at Keele Clinical Trials Unit will check your questionnaire responses and contact you to; either ask you to attend a screening visit at your GP practice or at your own home or to advise you that the next stage of the study is not suitable for you.

If you are not currently experiencing gout flares, we may ask you to contact us when you experience a gout flare if you are still interested in taking part in the study. Otherwise, no further contact will be made with you for participating in this study. By returning the questionnaire you are not agreeing to take part in the study.

What will happen to me if I take part?

If you would like to take part and your questionnaire responses suggest that the study is right for you, then you will be invited to attend a screening visit.

Screening visit: This will be held at your GP practice or at your own home, and you will be seen by a nurse or a trained researcher. You will have the opportunity to ask more about the study and, if you would like to take part, you will be asked to sign a consent form. The nurse or trained researcher will check your medical history, examine your joints, measure any lumps due to gout below the skin (if you have any), and take a blood sample of approximately 1 teaspoon of blood to measure your urate level and kidney function. They may measure your blood pressure at this visit if you wish for the next study visit to be conducted remotely i.e. over the phone. They will contact you a few days later to tell you whether the study is right for you. This will depend on your blood urate levels and kidney function.

If your blood results show the study is right for you, then appointment will be arranged with you approximately 1-2 weeks later by a nurse or a trained researcher for the first study visit. Depending on your preference this can be done face-to-face or remotely over the phone.

First study visit: This visit can take place face to face at your GP practice or at your home (if you are unable to attend your GP practice) or over the phone if there are restrictions on face-to-face visits in your area due to coronavirus. For this visit you will be asked to complete a questionnaire and provide a urine sample (if you opt for a telephone visit you will be asked to drop your urine sample into your GP practice at a later date.) If you opt for a face-to-face visit your height, weight, and blood pressure will be measured. If you have opted for a phone call then we would already have measured your blood pressure and we will allow you to record your own height and weight at your home if this is possible and let us know. You will be asked if you are still happy to take part and you will then be allocated at random to one of two treatments which are described below.

We have two different treatment regimes to compare, because we do not know which way of treating gout is best. To find out, we need to make comparisons between two different ways of treating gout. We put people into groups and give each group different treatment. To try and make sure the groups are the same to start with, each patient is put into a group by chance (randomly). The results are then compared between the groups.

Whichever group you are in, you will receive information from the research team about managing gout flares.

Treatment 1: Treat-to-target urate-lowering treatment: You will start on a low dose of a medication called allopurinol which is used regularly by doctors to lower blood urate levels. If you are currently taking allopurinol then your dose may be increased. You will then be seen approximately every 4 weeks by a practice nurse or another member of the GP surgery staff, at your GP practice and approximately 1 teaspoon of blood will be taken to check your urate levels. Your dose of allopurinol will then be increased until you reach the correct level of urate in the blood and the dose will then be maintained. If face-to-face visits are being restricted at your GP surgery or if you are not keen to attend due to concerns about coronavirus, your nurse or GP may be able to increase your allopurinol dose to 300 mg/day without doing any blood tests. However, it will not be possible to increase the dose of allopurinol to a higher dose without measuring the urate level in your blood. We are doing this because we know that most people require at least 300 mg allopurinol daily to achieve an acceptably low level of blood urate to dissolve away the urate crystals. Your right to refuse your dose being increased will be respected, and, if you experience any side effects you will be offered the choice to continue on a different urate-lowering treatment or you can discontinue the treatment altogether. If you have had side effects from allopurinol in the past but wish to take part in the study, you will be offered the choice to start on a different urate-lowering treatment called Febuxostat.

As starting on urate-lowering medicines can increase the risk of developing gout flares, we will commence you on an extra tablet for six months to reduce the risk of you developing gout flares. Your GP surgery will arrange for the prescriptions and these can be collected from your local NHS pharmacy.

Treatment 2: Usual GP care: You will be advised to consult your GP as usual and receive treatment for gout flares and urate lowering treatment according to your GP's usual practice.

Which group you are allocated to is made at random by a computer program at Keele Clinical Trials Unit. Like the flip of a coin, you have an equal chance of being allocated to one of the two groups. It is important to remember that everyone who takes part in the

study, whichever group they are in, is providing an equally valuable contribution. Both groups are essential to the success of this study.

Both treatment groups:

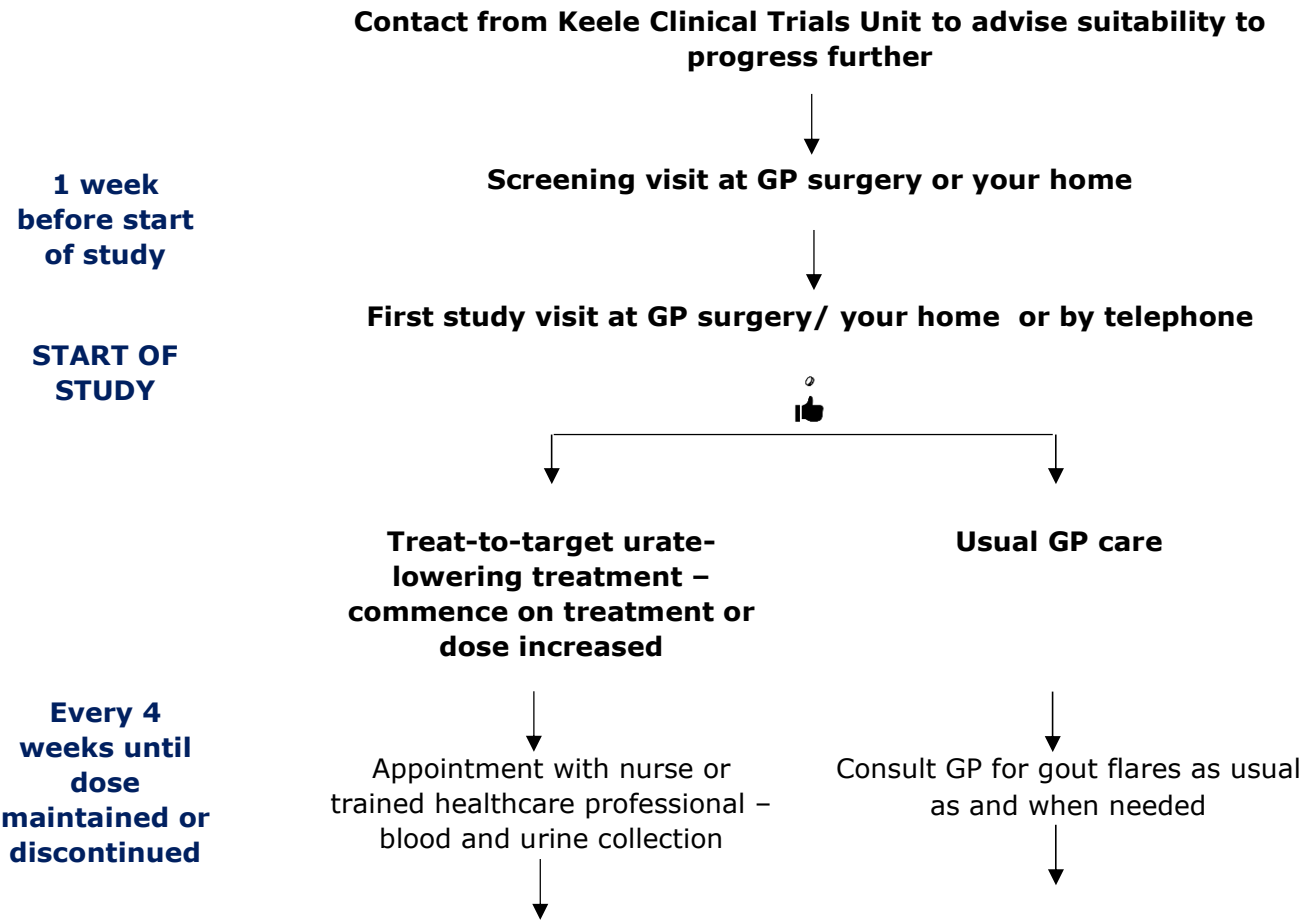
Yearly study visits: These visits will occur at your GP practice 1 year and 2 years after your starting in the study. If you are unable to attend the GP surgery, these visits can be arranged at your home. You will be asked to complete a questionnaire and blood and urine will be collected. Your height, weight, blood pressure will be measured and any lumps below the skin due to gout measured.

Information about gout flares: You will be asked to provide information on any gout flares that you experience during the study by providing information to Keele Clinical Trials Unit text message (SMS) response service on the first day of the flare.

If you do not wish to use a mobile phone text message (SMS), there is also an option to complete a gout flare diary online or to complete a paper gout flare diary and to return this to your GP practice or to Keele Clinical Trials Unit.

We will also ask you to complete either a paper or an online diary about your quality of life and treatment taken each time you experience a gout flare during the first two years of the study. Four years after you enter the study, with your consent, we will contact your GP surgery to ask about your gout and its treatment, and about any other illnesses in the previous 2 years.

Further information about what will happen as part of the study can be found on the flowchart on the next page.



Use SMS text message service when experiencing a gout flare and complete quality of life and treatment diary

(or complete a paper/online diary)

Use SMS text message service when experiencing a gout flare and complete quality of life and treatment diary

(or complete a paper/online diary)

1 year later

Attend research appointment at GP practice

Attend research appointment at GP practice

2 years later

Attend research appointment at GP practice

Attend research appointment at GP practice

4 years later

Contact made with your GP practice to ask about your gout and its treatment

END

OF STUDY

Expenses and Payment

You will not be paid to take part in the study. Travel expenses will be offered for any visits related to the study. If you receive treat-to-target urate-lowering treatment then extra prescription costs incurred as a result of the study will be paid back to you. This will stop after two years, or earlier if the study is stopped for some reason. If you incur a cost from sending text messages to the study team during a flare, it will be reimbursed.

What are the possible disadvantages and risks of taking part?

As with all research studies, there are potential benefits and risks to taking part.

Taking part will impact on your time and will vary according to which treatment you are allocated to. You will be asked to provide a blood sample at the screening and research appointments and will need additional blood tests if you are allocated to treatment-to-target. It is anticipated most people will require three or four such tests. During the taking of the blood test you may feel a sharp pin prick sensation but the rest of the procedure should be painless.

Any medications that will be advised to use for gout in this study will be currently available treatments that will be prescribed in line with current guidelines. As with any medication, the treatments for gout can sometimes cause side effects but it is rare to suffer any serious

upset. If you are allocated to treat-to-target urate-lowering treatment, we will offer medication to relieve your symptoms if you experience a gout flare.

What are the possible benefits of taking part?

We currently do not know the benefit to you by taking part in the study. However, your involvement will help us learn more about how gout should be treated and improve the care of patients with gout in the future.

What happens when the research study stops?

Your GP will be advised to continue to prescribe urate-lowering medicines at the end of the study if you receive the treat-to-target urate-lowering treatment if you agree to this. If you are allocated to usual GP care group you will be able to see your GP and start urate-lowering treatment if you so wish. You will also be able to see your GP for gout flares as normal. At this point, you will be able to discuss your options with your GP who will prescribe any further treatment in line with local policy. This will also be the case if the study stops early.

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. Their contact details are: T2T Trial Manager at Keele Clinical Trials Unit on 01782 732950 or email: sch-tr.t2tgout@nhs.net. If you have any questions or concerns about taking part in research you can also contact NHS England**:** Tel: 0300 311 2233, email: england.contactus@nhs.net.

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 University of Nottingham but you may have to pay your legal costs.

Will my taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence.

The University of Nottingham is the sponsor for this study based in the United Kingdom. If you decide only to complete the questionnaire and do not agree to be contacted further about the study, only the data you have provided up until this point will be used in the study analysis. If you join the study, we will use information collected from you and your medical records during the course of the research. This information will be kept strictly confidential, stored in a secure and locked office, and on a password protected database at Keele University and then the University of Nottingham at the end of the study.

Under the UK Data Protection act 2018 the University of Nottingham and Keele University are Joint Data Controllers (legally responsible for the data security), the University of Southampton is a data processor (processing your personal data on behalf of the University of Nottingham) and the Chief Investigator of this study (named above) is the Data

Custodian (manages access to the data). This means we are responsible for looking after your information and using it properly.

Your rights to access, change or move your information are limited as we need to manage your information in specific ways to comply with certain laws and for the research to be reliable and accurate. To safeguard your rights we will use the minimum personally – identifiable information possible.

You can find out more about how Nottingham and Keele use your information and read our privacy notices at:

Nottingham - https://www.nottingham.ac.uk/utilities/privacy/privacy.aspx

Keele - https://www.keele.ac.uk/privacynotices/privacynotice-researchparticipants/

The data collected for the study will be looked at and stored by authorised persons from the University of Nottingham who are organising the research and Keele University. They may also be looked at by authorised people from regulatory organisations 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.

Keele Clinical Trials Unit will use your name and contact details to contact you about the research study. The only people in Keele Clinical Trials Unit who will have access to information that identifies you will be people who need to contact you about the next stage of the research or who audit the data collection process. Research Nurses or a trained researcher based at the Universities of Nottingham, Keele or Southampton (depending on your location) who will be working on behalf of GP practice's as part of this study will also have access to your contact details in order to contact you about appointments. Your personal data will not be stored by them and will only be used at your GP practice.

The people who analyse the data that you provide, will not be able to identify you and will not be able to find out your name and contact details.

Your identifiable data will be securely stored by Keele Clinical Trials Unit and will not be used beyond these purposes other than by regional research nurses or a researcher in order to contact you about your appointments and to contact your GP practice to ask about your gout and its treatment. On joining the study, your information will be securely stored under a unique study number. Your questionnaire answers and research information collected on you (data) will only be associated with this number, not your personal details. We will also need this information as we need to follow up your medical records as part of the research, where we will ask your GP to provide medical information about your gout and its treatment. By signing the consent form you agree to the above.

Any information that you do provide which contains your personal identifiable details will be securely stored at Keele Clinical Trials Unit at Keele University but separately to the data that you provide.

Your contact information will be kept by the University of Nottingham for 6-12 months after the end of the study so that we are able to contact you about the findings of the study. This information will be kept separately from the research data collected and only those who need to will have access to it. All other data (research data) will be kept securely for 7 years. After this time your data will be disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team given permission by the data custodian will have access to your personal data.

In accordance with the University of Nottingham's, the Government's and our funders' policies we may share our research data with researchers in other Universities and organisations, including those in other countries, for research in health and social care. Sharing research data is important to allow peer scrutiny, re-use (and therefore avoiding duplication of research) and to understand the bigger picture in particular areas of research. Data sharing in this way is anonymised (so that you could not be identified).

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

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you withdraw we will no longer collect any information about you or from you but we will keep the information about you that we have already obtained as this information may have already been used in some analyses and may still be used in the final study analyses. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Involvement of the General Practitioner (GP)

Your GP will be informed that you are taking part in the study. If you are allocated to treat-to-target urate-lowering treatment then your GP will be advised that you will be seen by the practice nurse or trained healthcare professional for treatment of your gout.

What will happen to any samples I give?

Any blood or urine samples you provide will be analysed for urate and kidney function, in your local hospital laboratory in the same way as in usual NHS care. They will be destroyed immediately after analysis.

What will happen to the results of the research study?

After the study has finished and we have reviewed the results, the main findings from the study will be displayed on a poster in your GP practice and will be available on the study website www.keele.ac.uk/t2t

The results of this study will also be shared at medical conferences and through publication in academic journals which are read by a large number of health professionals. You will not be identified individually in any report or publication.

Who is organising and funding the research?

This research is being organised by the University of Nottingham in collaboration with Keele clinical trials unit and the University of Southampton. The treat-to-target study is funded by the National Institute of Health Research (NIHR) Health Technology Assessment (HTA) programme.

Who has reviewed the study?

All research in healthcare is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by North West-Liverpool East Research Ethics Committee, REC Reference: 19/NW/0310.

Further information and contact details

If you have any questions, or would like any further information, please contact:

Trial Manager, Keele Clinical Trials Unit. **Tel: 01782 732950**

Email: sch-tr.t2tgout@nhs.net

Chief Investigator: Dr A Abhishek, University of Nottingham, **Tel: 01782 732950**

Thank you for taking the time to read this information leaflet and for considering taking part in this study.

This study is funded by the National Institute for Health Research (NIHR) Health Technology Assessment Programme (17/82/02). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and social care.

FUNDED BY NIHR | National Institute for Health Research