PATIENT INFORMATION SHEET

The role of ultrasound compared to biopsy of temporal arteries in the diagnosis and management of giant cell arteritis (TABUL)

We would like you to consider this research study and then decide whether or not you wish to take part. Before you decide whether to participate or not 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 and to decide whether or not you wish to take part.

1. What is the purpose of this study?

Our study will examine the role of ultrasound in helping to diagnose Giant Cell Arteritis (GCA). It causes narrowing and blockage of some of these blood vessels; it can cause severe headache and in some cases may affect eyesight. It is important that a prompt diagnosis of GCA can be made in order to start treatment with steroid tablets or injections. Currently there is no test that is 100% accurate for diagnosing GCA.

To help to confirm a diagnosis of GCA, the patient will usually have a biopsy of a temporal artery (a minor surgical procedure performed under local anaesthetic to remove a 1 to 3 centimetre sample of one of the arteries to the scalp). The examination of the biopsy sample usually confirms that the patient has GCA and steroid treatment can be continued. However, some patients with GCA will have a normal biopsy result. For these patients with a normal biopsy result it is difficult to confirm if they do or don't have GCA and whether or not steroid treatment should be continued.

The main study

It is important to find better ways of diagnosing GCA to ensure that more patients are treated appropriately. Another test that may help in diagnosing GCA is examination of ultrasound scans of the arteries in the side of the head and under the arms. Ultrasound does not involve surgery; it is a simple test which can be performed in a radiology department. Gel is applied to both sides of the head and under each arm. A sound probe is placed over the artery at each of these areas to produce the scan for expert examination

The sub-studies

We are asking you to take part in the main study described above, but in addition, there are a number of separate sub-studies that you can also choose to participate in, to look at immune abnormalities in GCA; make an educational website for doctors to use and to store ultrasound images, samples and other data in a Biobank for future studies.

2. Why have I been invited?

You have been chosen because you have been suffering a new onset of headache which is suspected as being giant cell arteritis and the doctors looking after you have decided that you need a biopsy of your temporal artery to clarify the diagnosis.

3. Do I have to take part?

It is up to you to decide whether or not to take part. You are free to withdraw at any time and without giving a reason. If you decide to take part we will ask you to sign a consent form indicating your willingness to participate in the study. Any current or future healthcare that you receive will not be affected by deciding whether or not to take part in the study. Taking part in the study is voluntary.

4. What will happen if I take part?

If you take part in the study, you will need to attend for an ultrasound scan of your scalp and armpit arteries before the planned biopsy. The scan will take about 30 minutes to complete. At the first study visit, you will be assessed by the study nurse or doctor and asked to complete questionnaires about your health; you will be reviewed two weeks (study visit 2) and six months (final study visit) later where the study nurse or doctor will repeat the assessment and ask you to complete the same health questionnaires. Your ultrasound scan result will not be disclosed to you or to the doctors and nurses looking after you. If you agree to take part in any sub-studies, you will also need to give blood samples on each of the 3 study visits.

Participating in the TABUL study will not affect the care you receive from the National Health Service (NHS).

5. What do I have to do?

The main study

By the time you read this, you will have been referred to hospital for a possible diagnosis of GCA. The doctors looking after you will have told you about the study and asked your

permission to contact the study nurse or study doctor. We have given you this information sheet about the study. The study nurse or doctor will get in touch with you; they will either see you on the day of your scheduled hospital visit, or telephone you so that they can give you more information about the study. The research nurse or doctor will arrange to see you after you have had an opportunity to read the information and ask any questions. At this time you can ask further questions about the study, if you decide to take part in the study, at this point you will be asked to sign a consent form (study visit 1). A friend or relative can sign the consent form on your behalf if needed. If you agree to participate in the study, you will be assessed by the study nurse or doctor and asked to complete a questionnaire. An appointment will be made for you to have the ultrasound scan before your biopsy. We will make sure that your biopsy has been arranged. You would usually be attending hospital regularly after the biopsy to check on your health and adjust your treatment. You will be asked to attend for 2 further follow up visits after 2 weeks (study visit 2) and after 6 months (final study visit). On each study visit, the study nurse or doctor will assess you. We will ask you questions about your condition and how it affects your daily life, using standard questionnaires. We expect the first study visit to last about 60-90 minutes, and for each of the 2 subsequent study visits to last between 45-60 minutes. The doctor or nurse in the clinic will complete specialised clinical questionnaires, to assess your diagnosis, but we will also ask you to complete health questionnaire on your ability to carry out normal activities of daily living and your quality of life. We anticipate that it will take about 5-10 minutes for you to complete the questionnaires.

You will have an ultrasound scan of your scalp arteries (temporal arteries) and armpit arteries (axillary arteries) in addition to your routine biopsy of one temporal artery. The ultrasound scan is entirely painless. It will involve applying gel to the both sides of your head, and both armpits. The person performing the scan will place a sound probe over these 4 sites in order to identify the arteries. The probe will be used to record the images, and test each artery for signs of swelling, blockage and narrowing. The probe will be moved over the arteries and different settings will be applied using the dials on the machine to get the best picture. We hope to test the value of performing an ultrasound scan of these 4 arteries as an alternative to a biopsy of one temporal artery. We expect the scan to take about 30 minutes to complete. For training purposes, and if you are willing to do so, more than one scan may be performed.

We will store the biopsy samples and images of the ultrasound scans in one centre (Oxford), so that we can use the material to make sure that all the different hospitals taking part in the study are performing and interpreting the biopsy and scan results according to a high standard of accuracy

Sub studies

We would like to perform some further tests on your biopsy and blood samples we collect from you so that we can gain a better understanding of the disease. In addition to the main study, we are planning to undertake a number of sub studies, making use of the biopsy sample that will normally be taken, as well as the video images of the scans and extra blood samples which we will ask you to provide on each of the 3 study visits. These sub studies are optional. You can take part in the main study and choose not to take part in the sub studies. The sub studies will look at the immune abnormalities in the biopsy sample and blood samples to try to determine what type of cells and inflammatory chemicals are responsible for the condition. This will involve processing the biopsy sample and blood samples to extract the cells, measure the inflammatory chemicals in the blood and look at the biopsy in detail, using special attaining techniques. If you agree to the sub-studies, we will take the additional blood samples (maximum total of 85 ml):

1. **Study Visit 1** - 6 tubes of blood (approx. 35 ml total, equivalent to about 7 teaspoonfuls).
2. **Study Visit 2 (2 weeks)** - 5 tubes of blood (approx. 25 ml total, equivalent to about 5 teaspoonfuls).
3. **Study Visit 3 (6 months)** - 5 tubes of blood (approx. 25 ml total, equivalent to about 5 teaspoonfuls).

Please note that these will be in addition to your routine blood samples at each visit.

We would like to make use of the video images of the scans and of the images of the biopsy samples in order to develop and test the usefulness of a training website to teach other doctors about the best way to diagnose temporal arteritis. No personal details will be used on the website.

We would like your permission to store your samples of blood and your biopsy in a Biobank for future related studies

We will remove your personal details from all research samples so that they are all anonymous and your personal details will remain confidential. However, it will be possible to link the clinical and laboratory details through a unique laboratory code to enable us compare your clinical state with the laboratory findings. Your blood samples will be stored in a laboratory freezer until used.

We would like to store some of your DNA extracted from the blood samples to form part of our Biobank that we can use in future genetic studies. This is purely for research purposes

and you will not be told the results of the tests on your samples. The anonymous genetic information may be shared with other research groups conducting similar investigations.

6. Expenses and payments

If you incur travel expenses in order to attend especially for the ultrasound scan this extra appointment will be reimbursed on request.

7. What are the possible benefits of taking part?

Your condition of suspected giant cell arteritis will be treated by the doctors in hospital in the normal way, using widely recognised means. You will not directly benefit from taking part in this study but the information we get from this study will help improve future treatment of people with suspected giant cell arteritis.

8. What are the possible risks of taking part?

Ultrasound is a safe technique. The temporal artery biopsy procedure would be part of routine care so you would be undergoing this procedure whether you decide to take part in the study or not. Complications following a temporal artery biopsy are rare, but include bleeding, swelling over an artery due to formation of a blood clot (haematoma), damage to branches of the facial nerve, failure to identify the artery, development of infection at the biopsy site, wound breakdown and very rarely scalp necrosis.

9. Will my taking part be kept confidential?

All patient information is stored on password protected computer databases and in locked filing cabinets and will only be accessible to the TABUL research team and regulatory authorities for auditing and monitoring purposes. You will be allocated a unique study number and staff not directly involved with you will know you only by this number. When the results of the study are reported, individuals who have taken part will not be identified in any way. Again we must emphasise that none of your samples will identify you in any way as we will use your unique study number when storing them. Responsible members of the University of Oxford or the local Hospital NHS Trust may be given access to data for monitoring or audit of the study to ensure we are complying with regulations.

10. What if I change my mind about taking part?

If you decide to withdraw from the study, your standard of care will not be affected. You will **still** be asked to attend the routine follow-up clinics required by your doctor and hospital as part of your standard care. These follow up clinics will not be part of 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.

11. What if there is a problem?

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact Dr Raashid Luqmani on XXXX or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on XXXX or the head of CTRG, email XXXX.

The University has arrangements in place to provide for harm arising from participation in the study for which the University is the Research Sponsor. NHS indemnity operates in respect of any clinical treatment with which you are provided.

12. Will my GP be informed of my involvement in the study?

Yes. We will send your GP a brief letter informing them of your participation in the study.

13. What will happen to any samples I give?

The video images of your scans, tissue and blood samples collected for the TABUL study will be sent to the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Science, in Oxford, for analysis. Samples of blood will be stored for future studies, including DNA studies to learn more about the nature of giant cell arteritis. None of these will identify you in any way as we will use your unique study number when storing them. However, if your local hospital requires the biopsy sample to be returned for clinical care, we will be able to trace the sample from the unique study number, supplied by your hospital, so that the sample can be returned. We will use the video images of the scans and the biopsy samples to train the investigators in the study to make sure that we maintain a high standard of quality control. In order to do this, at least 2 experts trained in ultrasound from the study panel will independently review all the video images of the scans; 1 or 2 expert pathologists from the study panel will independently review all the biopsy slides. If there is a disagreement with the findings of the local investigator, this will be discussed.

If you agree to take part in the sub-studies, we will store your biopsy sample and blood samples in a Biobank at oxford. All specimens will be carefully catalogued and maintained in a facility which is fully compliant with the requirements of the Human Tissue Act. This will allow us to safely and securely keep your samples in a freezer, for use in future studies,

which will be reviewed and approved by a Research Ethics Committee, before we make use of these specimens.

14. How will the information I provide be used?

We plan to publish the results in a health journal so others can read about and learn from the results of the study.

15. Who is organising and funding the research?

This nationwide trial is being funded through the Health Technology Assessment (HTA) Programme, which is part of the Department of Health. You can access information about them on the HTA website (www.hta.nhs.uk).

The Nuffield Department of Orthopaedic, Rheumatology & Musculoskeletal Sciences (www.ndorms.ox.ac.uk) a department of the University of Oxford, in Oxford will undertake the day to day running of the trial, under the supervision of Dr Raashid Luqmani. The University of Oxford will act as a sponsor for the study and will be responsible for the governance of the trial. The Sheffield Clinical Trials Unit will be responsible for collecting and monitoring the information generated.

16. Who has reviewed this study?

The Berkshire Research Ethics Committee have reviewed the study and given it a favourable opinion. In addition your local NHS hospital Trust have and your local rheumatologist or ophthalmologist have approved the study.

17. Further Information

If you require more information about this study please call one of the telephone numbers provided to speak to a clinical member of the research team or, alternatively look at the clinical trials website:

http://clinicaltrials.gov/ct2/show/NCT00974883.

Thank you for reading this.

If you have any questions or would like any more information please contact the TABUL Office by phone:

XXXX (XXXX) or XXXX (XXXX)

Or email XXXX

Please keep this information sheet for your records.

If you agree to enter the study, please sign the attached consent form and we will return a copy to you