TO BE PRINTED ON LOCAL TRUST HEADED PAPER

PATIENT (16-18YRS) INFORMATION SHEET

Study Title
Short course daily prednisolone therapy at the time of upper respiratory tract infection in children with relapsing steroid sensitive nephrotic syndrome; the PREDNOS 2 study

Invitation to take part in this research study

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. Please take time to read the following information carefully and discuss it with others and your doctor if you wish. Ask 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.

Part 1 tells you the purpose of this study and what will happen to you if you take part.

Part 2 gives you more detailed information about the conduct of the study.

Part 1

What is the purpose of the study?

Children and young adults with nephrotic syndrome suffer from disease relapses, where the protein in the urine returns. When these occur, treatment with high dose prednisolone is commenced and this may be associated with a number of side-effects. For this reason, every effort is made to prevent relapses from happening. This generally involves the use of either low dose every other day prednisolone, or other drugs such as levamisole, ciclosporin or mycophenolate mofetil.
It is well known that relapses may be caused by upper respiratory tract infection (URTI– the common cold). Three small studies performed in the developing world (India and Sri Lanka) have shown that if a short course of daily steroid treatment is commenced when children and young adults develop an URTI, this reduces the risk of a relapse developing. The purpose of this study is to see whether giving a six day course of daily prednisolone when children and young adults develop an URTI prevents relapses from developing: we will study this in a large population of UK children and young adults with relapsing nephrotic syndrome. The study is being conducted by the kidney specialists in every children's kidney unit in the UK and has been selected for funding by the National Institute for Health Research.

Why have I been chosen?

You have relapsing nephrotic syndrome and have had at least two relapses in the past 12 months. We are asking 360 patients from hospitals in the United Kingdom to take part.

Do I have to take part?
No, taking part in the research is entirely voluntary. It is up to you and your decision will not affect the standard of care you receive. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care you receive. If you do not take part or you withdraw from the study, you will receive your consultant's usual treatment for nephrotic syndrome.

What will happen to me if I take part?
Once you have agreed to participate in the study, you will receive a supply of study medicines – a pot of tablets which will be sent by Royal Mail Special Delivery to your family home. One half of participants will receive a pot of prednisolone and the other half will receive a pot of identical placebo (a dummy medicine, with no activity or side effects). A computer will decide whether you receive active prednisolone or the placebo – a bit like tossing a coin. Neither you or your doctor will know whether you have been given the prednisolone or the placebo, though this information can be found out in case of an emergency. This is to make the study the best possible test of which treatment is better. Each time you develop an URTI during the 12 month study we will ask you to commence a six day course of study medicine. For this to happen, you must have had two of the following symptoms for at least 24 hours: sore throat, ear pain/discharge, runny nose, cough (dry or barking), hoarse voice or fever above 37^{o}C. We will provide you with an electronic thermometer and clear written information about these symptoms. We will also provide you with clear written information about exactly how many tablets you should take – this will depend on your weight and height, as well as the dose of prednisolone that you may already be receiving.
We will monitor your progress in the usual way, through telephone calls with your local doctor and/or the nurse responsible for your care.

All participants will be followed up in clinic at 3, 6, 9, and 12 months to assess their progress.

At one of the study visits a single 10ml (two teaspoon) blood sample will be collected from you to look at genetic changes associated with nephrotic syndrome. Where possible, we will collect this at a time when you are having blood tests for routine clinical purposes. If you do not want to have a blood sample collected for the purposes of the study that is fine, you can still take part in the study without giving a blood sample. There is increasing information suggesting that nephrotic syndrome may be a genetic disease and the blood sample will be used to analyse the DNA from all participants in the study in order to see if there is a common genetic mutation (minor change) and also to see whether we can understand the cause of the disease.

We will ask your parent/guardian to complete four short questionnaires about your behaviour and quality of life at the beginning of the study and at 3, 6, 9, 12 months. This should take less than 20 minutes of their time on each occasion. These questionnaires will only be identified by your unique study number and date of birth in the month/year format to maintain confidentiality.

The rest of your treatment will be usual treatment for relapsing nephrotic syndrome. You will be asked to test your urine for protein in the usual way to see if the nephrotic syndrome is coming back. You will record the results in your patient diary and bring it with you to regular check-ups with your doctor. In your patient diary we will also ask you to record whether you have been unwell in any way, and record any visits to your GP or hospital, along with any other medicines that you have given to you. Study follow-up visits will be at baseline and months 3, 6, 9 and 12. See Table 1 below:

Information from the diary that you complete will be recorded in your medical record and on the study assessment forms during the study follow-up visits.

Table 1

Study Follow-up Visits	**1**	**2**	**3**	**4**	**5**
Baseline/Months	Baseline	Month 3	Month 6	Month 9	Month 12
Regular checkups that are part of the usual treatment for nephrotic syndrome (including documentation of recent medical/drug history, any parental concerns, physical exam, height and weight, and blood pressure check)	Yes	Yes	Yes	Yes	Yes
Blood sample for study	x (can be at any time in 12 month study period)				
Four short questionnaires about your behaviour and quality of life (parent completed).	Yes	Yes	Yes	Yes	Yes

What is the drug or procedure that is being tested?
Prednisolone is a steroid drug which suppresses the immune system. Prednisolone is the standard treatment for relapsing nephrotic syndrome.

What are the alternative treatments available?
At present, the large majority of children and young adults are given no extra treatment when they develop an URTI. There is no agreed standard therapy, though it is hoped that if the results of this study show a benefit to giving a short course of prednisolone, then this will become standard therapy nationally.

What are the side effects of the treatment?
Prednisolone treatment can cause side-effects, including a puffy face and body and mood changes. Other side effects include weight gain, skin problems, osteoporosis (thinning of the bones), sore throat or mouth and an increased risk of infection.

Patients taking prednisolone should avoid coming into contact with chickenpox, should not suddenly stop taking prednisolone and should carry a steroid card that explains they are taking prednisolone, a steroid drug. You should contact your consultant paediatrician straight away if you have come into contact with chickenpox unless you have been told this is not necessary because you are immune to chickenpox. This should be through contacting the consultant's secretary or nurse specialist during office hours or the hospital ward at other times.

Patients taking prednisolone should avoid all live vaccines. Therefore during the course of the study all live vaccines should be avoided. Routine live vaccines such as MMR can be given once immunosuppressive therapy has been stopped. Your GP will be informed of this.

What are the possible disadvantages and risks of taking part?
The purpose of the study is to see whether giving a short course of prednisolone when participants develop an URTI prevents them from developing a full relapse, which would need treatment with a long course of high dose prednisolone. If this is not the case, then those participants who received prednisolone at the time of an URTI will have received this short course of prednisolone unnecessarily and there is a very small chance that this may be associated with minor side-effects. All participants will be monitored for side-effects and if there is any concern that these are in any way associated with the study then you could be withdrawn from the study.

What are the possible benefits of taking part?
Participants in research studies such as this receive very close monitoring, which will be advantageous to your general health. The information we get from the study may help us to improve the treatment of all children and young adults in the UK with nephrotic syndrome in the future.

What if new information becomes available?
Sometimes during the course of a research study, new information becomes available about the treatment that is being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, your research doctor will make arrangements for your care to continue. If you decide you wish to continue in the study you will be asked to sign an updated consent form. Your research doctor may also discontinue you from the study if your safety is compromised at any time.

What happens when the research study stops?
When the research study stops the results of the study will be published and the information we get from the study may help us to improve the treatment of children and young adults presenting with relapsing nephrotic syndrome in the future. If we discover that daily prednisolone treatment at the time of URTI does reduce relapse it will be used in future as standard care. When the research study stops and the study results have been published you can be told which arm of the study you were in if you are interested.

What if there is a problem?
Any complaint about the way you have been dealt with during this study or any possible harm you might suffer will be addressed. The detailed information is given in Part 2.

Will my taking part in the study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The detailed information is given in Part 2.

Thank you for reading so far – if you are still interested, please go to Part 2

Part 2

What if relevant new information becomes available?
Sometimes, during the course of a research project, new information becomes available about the treatment(s) being studied. If this happens, your study doctor will discuss how this affects your care and participation in the PREDNOS 2 study. Your study doctor might consider that you should continue in the study or withdraw. Either way, he/she will explain the reasons and arrange for your care to continue. If you decide to continue in the study you may be asked to sign an updated consent form. If the study is stopped for any other reason, your doctor would, again, tell you and arrange your continuing care.

What will happen if I do not want to carry on with the study?
You can decide not to continue with study at any time but, if you do, we would still like to follow-up your progress and your data would remain on file and be included in the final study analysis unless you request that they should not be.

What if there is a problem?
If you are harmed due to someone's negligence, then you may have grounds for a legal action but may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms should be available to you. Taking part in this study would not affect your legal rights.

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. The contact details for the PREDNOS 2 Chief Investigator are: Dr Martin Christian, Telephone 0115 924 9924 x63832. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

Will my taking part in the study be kept confidential?
If you decide to take part in the PREDNOS 2 study all information which is collected about you during the course of the research will be kept strictly confidential in the same way as your medical records. Information about your disease and progress will be sent by your doctors to the PREDNOS 2 study office at the University of Birmingham Clinical Trials Unit, on paper and electronically, where it will be securely stored under the provisions of the General Data Protection Regulation and Data Protection Act 2018. If you consent to taking part in this study, your GP and the other doctors involved in your clinical care will be notified of your participation in the PREDNOS 2 study and kept informed of your progress. With your permission, your relevant medical records may be inspected by authorised individuals from the Birmingham Clinical Trials Unit or your hospital. They may also be looked at by the study team and regulatory authorities. The purpose of this is to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and will do their best to meet this duty. If you consent to taking part in this study a copy of the consent form will be faxed to the Birmingham Children's Hospital Pharmacy Department who will send the study medication direct to your home.

In line with clinical trial guidelines, at the end of the study, the data will need to be securely archived for up to 25 years. Arrangements for confidential destruction will then be made. Should you withdraw consent for your data to be used, it will be confidentially destroyed.

What will happen to the blood sample I give?
The blood sample will, where possible, be collected at a time when you are having a blood test performed for routine clinical purposes. (If you do not want to have a blood sample collected for the purposes of the study that is fine, you can still take part in the study without giving a blood sample). Following collection, the sample will be sent to the Institute of Child Health, London (Prof Detlef Bockenhauer's laboratory), where DNA will be isolated. Half will be used in experiments to see if there is a genetic cause for nephrotic syndrome (by Prof Detlef Bockenhauer and Prof Robert Kleta at Great Ormond Street Hospital) and the other half will be used by Dr Ania Koziell at Kings College, London and Professor Moin Saleem at Bristol University in other experiments using different techniques to look at genetic changes in relapsing nephrotic syndrome. Following completion of this work, any remaining DNA samples will be retained in the laboratories of Prof Bockenhauer/Prof Kleta in London and/or

Dr Koziell/Professor Saleem in London and Bristol for use in future research projects investigating genetic factors and disease mechanisms in steroid sensitive nephrotic syndrome which may arise as a result of this work. Any such studies on these samples would require Research Ethics Committee approval. Your DNA sample will be identified only by your study number and date of birth in the month/year format; the sample will not be labelled with any personal information.

What will happen to the results of the research study?
Once the study has finished the results from all patients who took part in the study will be published in a scientific journal. The publication will appear when all the participants have completed the study and the results have been analysed. Your doctor can provide you with a copy of this publication if you are interested. We will also publicise the results on the study's website. Only anonymous data will be published and your name will not appear in any report, presentation or publication.

Who is organising and funding the research?
The PREDNOS 2 study is being co-ordinated by the Birmingham Clinical Trials Unit at the University of Birmingham and is sponsored by the University of Birmingham and Manchester University NHS Foundation Trust. The study Chief Investigator is Dr Martin Christian at Nottingham Children's Hospital. The study is supported by the British Association for Paediatric Nephrology and the Clinical Research Network for Children. The study is being funded by National Institute for Health Research Health Technology Assessment Programme. The research has been reviewed and approved by all these organisations. Your doctor will not be paid for including you in this study.

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 favourable opinion by North West – GM Central Research Ethics Committee. Research Ethics Committees include healthcare professionals as well as non-medical people, and are completely independent from anyone organising the study.

Where can I get further information?
For queries about the study or for further information please contact:

Dr Martin Christian, Telephone 0115 924 9924 x63832, PREDNOS 2 Chief Investigator

<Insert Local PI Name>, Telephone <Insert Local PI Tel. No.>, PREDNOS 2 Principal Local Investigator

The PREDNOS 2 study co-ordinating centre is located at the Birmingham Clinical Trials Unit, Institute of Applied Health Research, Public Health Building, University of Birmingham, Edgbaston, Birmingham B15 2TT. Tel 0121 415 9131, Fax: 0121 415 9135, Web address: www.birmingham.ac.uk/PREDNOS2.

Thank you for considering participation in this study.

You will be given a copy of this information sheet and your signed consent form to keep if you decide that you wish to take part in the study.