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Dear Behcet's Society member

CLINICAL TRIAL OF INTEREST TO PATIENTS WITH BEHCET'S DISEASE

We are writing to you to let you know about a clinical trial just for patients with Behcet's Disease and we wish everyone who would like to take part, wherever they live, to have the opportunity to do so.

1. Study Title: Can the addition of interferon alpha to therapy for Behcet's disease, reduce the risk of severe disease relapse over several years?

2. Invitation: 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 and discuss it with friends, relatives and your GP if you wish as well as the Consultant looking after your Behcet's Disease. Thank you for reading this.

3. What is the purpose of the study?: As you will know if you suffer from Behcet's disease, this can cause you several different types of problems as well as involving the eyes. Treatment often requires steroid tablets and other drugs which aim to suppress the immune system, which is overacting for an unknown reason, and thereby try and prevent further damage occurring. Unfortunately even on this treatment, many of you do not have your disease completely controlled and relapses occur which often require treatment with even higher levels of these drugs with all their accompanying side effects. Interferon alpha is a naturally occurring substance which has the ability to suppress the immune system. Several small studies (which altogether have treated over 450 patients) have suggested that patients with Behcet's disease may be helped by interferon alpha and that with just a six month course, long term disease suppression may occur. On the other hand, interferon alpha has to be given by injection once a week and does have side effects of its own. At the present time, interferon alpha is not readily available to any patient with Behcet's disease in the UK but will be free for the purposes of this trial. This study aims to answer the question as to whether interferon alpha is really helpful to you or not in the long term and whether its side effects are worth it.

4. Why are we writing to you?: In order to really know the answer to this question, we are inviting all patients with Behcet's disease who are eligible and would like to take part in this study. 140 patients from the UK will be invited to participate. You do not have to be a patient at Moorfields Eye Hospital to be involved as we are working with hospitals all over the country nor do you have to have eye involvement with your Behcet's Disease as other manifestations of Behcet's disease can be severe enough to warrant treatment with steroid and other immunosuppressive drugs.

5. Do I have to take part?: It is up to you to decide whether or not you wish to take part. If you do decide that you would like more information and would like to consider taking part if you are eligible, we will need to be in contact with the doctors looking after you. We will need you to contact us (see contact details at the

end of the letter) with this information. To be eligible you need to be taking certain immunosuppressive drugs and steroids. We will also check your medical history to ensure that the study is suitable for you.

6. What will happen to me if I take part?: If you agree to take part, you will be assessed and allocated to additional treatment with injections of interferon or not, by an independent system that will reliably allocate equal numbers of patients to each group. You do not need to agree to take part when you have your next clinic visit but you could defer it to another clinic visit if you wish to. We do not allocate these treatments at the clinic visit in which you agree to take part, as this takes time and will be done over the next week or at a convenient time. You need to be aware that if you are allocated to the non-additional treatment arm, you will not be given interferon-alpha injections but you will be monitored in exactly the same way as the patients who are. Your usual treatment will continue in the normal way whichever group you are in. The injections (prescribed for half of the patients) are given once a week for 6 months and we will teach you how to do this. Some injections will be given in the clinic when you attend and then we will be able to give you the drug to take home for the weeks in between the clinic visits. The injections are only given for 6 months and then stopped. If you develop a disease relapse during this time, you will be treated in exactly the same way whether or not you are on interferon alpha and as if you were attending the clinic in the usual way. No additional clinic visits will be required if you are involved in the trial, over and above the need for your usual clinical attendances. You may need to attend your usual clinic as well in between times and that is not a problem – everyone who is involved in your care will know if you are given interferon alpha. If you are female and of child bearing age, you must use a reliable contraceptive while you are on interferon alpha.

The panel of doctor's involved in the trial includes eye doctors, physicians who are expert in the management of all types of problems with Behcet's Disease and a physician who is an expert on the use of interferon alpha. The study nurse is a dedicated nurse for the study and is there to help support all the patients in the trial. There is an independent monitoring committee who will have access to all the details of the trial and will particularly be involved in monitoring patient safety.

7. What do I have to do?: All patients enrolled in the trial will need to have a study visit documented every 3 to 6 months for 3 - 4 years which can be in your own hospital if they are happy to take part or at a Centre near you. This is to fully document what is happening to those that have and have not had interferon alpha to determine if there is any effect both in the short and longer term. You will need some blood tests done while on the interferon alpha and over the study period. Some of these will be monitoring tests for the effects of the drug. We will also take some base line blood samples to look at the genes controlling your cytokine production to see if we can associate any of these with the treatment outcome.

8. What is the drug being tested?: The drug is called interferon alpha 2b which is a naturally occurring substance which has the ability to suppress the immune system which is overactive in diseases like Behcet's disease and causes the harmful inflammation.

9. What are the alternatives for treatment?: Most patients with Behcet's disease who have active disease are treated with a combination of steroid tablets and /or other drugs such as cyclosporin, mycophenolate (cellcept) and azathioprine which suppress the immune system. Many of you will have experienced many unpleasant side effects of the drugs especially when you are on high doses to treat active disease.

10. What are the side effects of any treatment received while taking part?: On the day of injection you may experience flu like symptoms which can be managed and controlled with paracetamol tablets and the injection site may be slightly tender. Both of these effects are mild and should improve with time. As with the other drugs you are taking, we need you to have monthly blood tests to ensure that your immune system is not over-suppressed.

11. What are the possible disadvantages of taking part?: All of you are under regular medical care for your Behcet's disease and this study involves you attending for a study visit every 3 months for the first 6 months, then 6 monthly for the next 3 - 4 years. The treatment with interferon alpha involves you giving yourself a small injection just under your skin every week for 6 months.

12. What are the possible benefits of taking part?: If this study shows that those of you who had the interferon alpha did much better than those that did not, we would aim to get this treatment available to everyone. If it does not, then we will have answered this question and there is no further point in any patients being given it. The main aim is to try and get you off needing drugs such as cyclosporin, azathioprine, methotrexate, mycophenolate and to use steroids at a maximum dose of 10 mg per day or hopefully much less or not at all, and yet still keep your disease under long term control.

13. Will my taking part in this study be kept confidential?: During the course of the study we need to keep all the information about your disease and its treatment as we do in the outpatient clinic. All the study records are kept in a locked filing cabinet in the Trial office and you will be allocated a study number which will be used wherever possible to maintain your confidentiality. It is essential for us to notify your GP if you are given interferon alpha in case you develop symptoms that are related to this.

14. What will happen to the results of the research study?: The information about all the patients in the study will be carefully analysed to see if the benefits of the interferon are significant and considerably outweigh the disadvantages. If so, we will aim to get the interferon available to everyone who needs it and the best way of doing this is to present this information to all the doctors involved in the management of patients with Behcet's disease. This is done by presentation of the results at meetings and by publishing the information in medical journals. No patient is individually identified in this but the effects on the whole group determined. This will all be written in medical language but the significant results will be put in lay terms and sent to the Behcet's Society for distribution to its members who are largely sufferers of this disease.

15. Who is organising and funding the research?: This study is carried out independently of the drug company that makes interferon and they are not involved in any analysis of the results. The study is funded by the Moulton Charitable Trust and organised through the Institute of Ophthalmology and Moorfields Eye Hospital. It will be possible to contribute some money towards your travelling expenses if you need it during the time of the trial.

16. Who has reviewed this study?: This study has been approved by the Oxford Multicentre Research Ethics Committee and Local Research Ethics Committee at each hospital involved.

17. Contact for further information: The study doctor is Professor Susan Lightman and the study nurse is Helen Heath - She can be contacted via Professor Lightman's secretary/ PA on 020 7566 2252 or 020 7566 2266 where there is also an answer-phone to take messages if they are not immediately available. As soon as Helen is available, she will call you back.

Thank you for considering taking part in this study.



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